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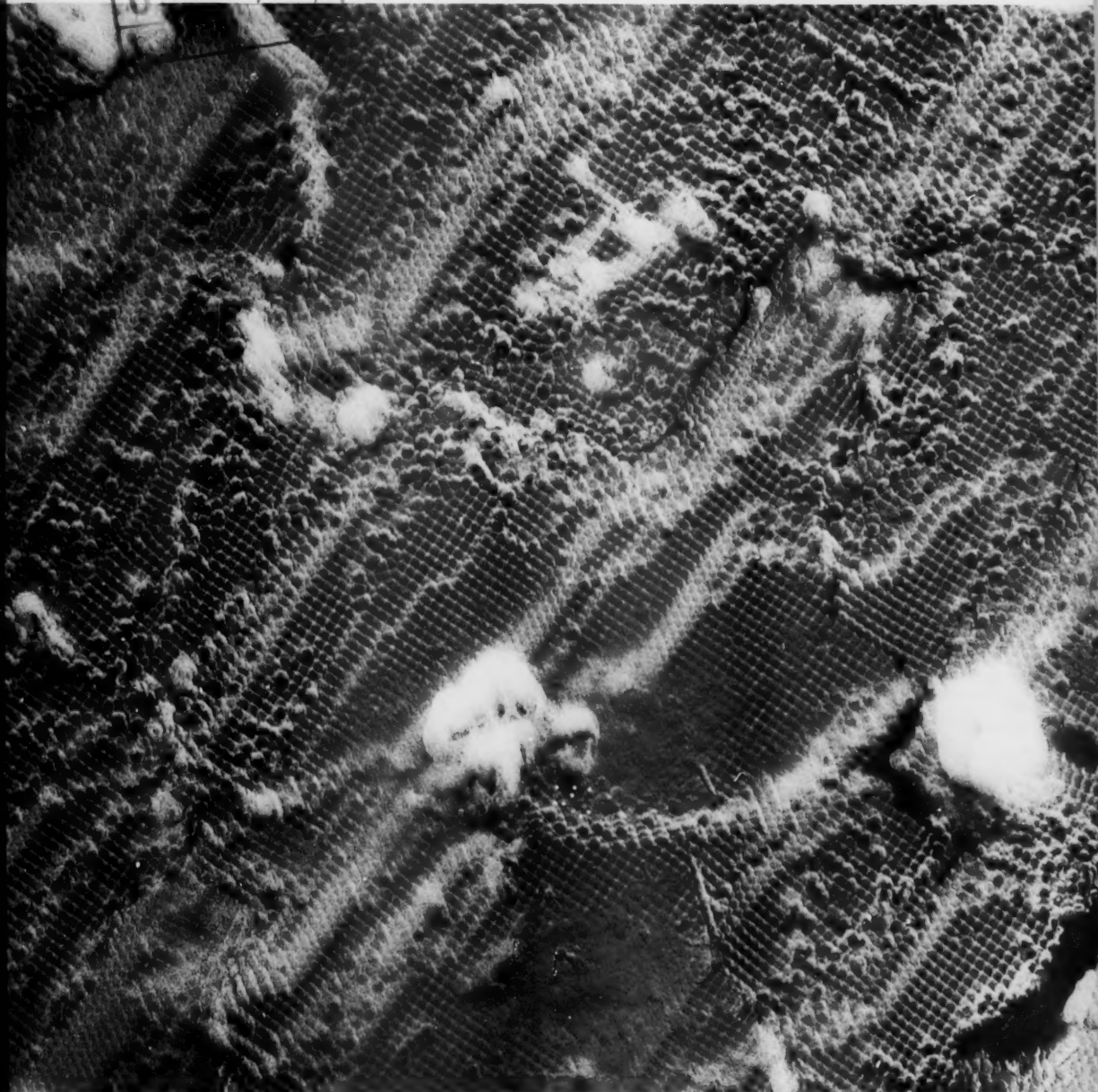
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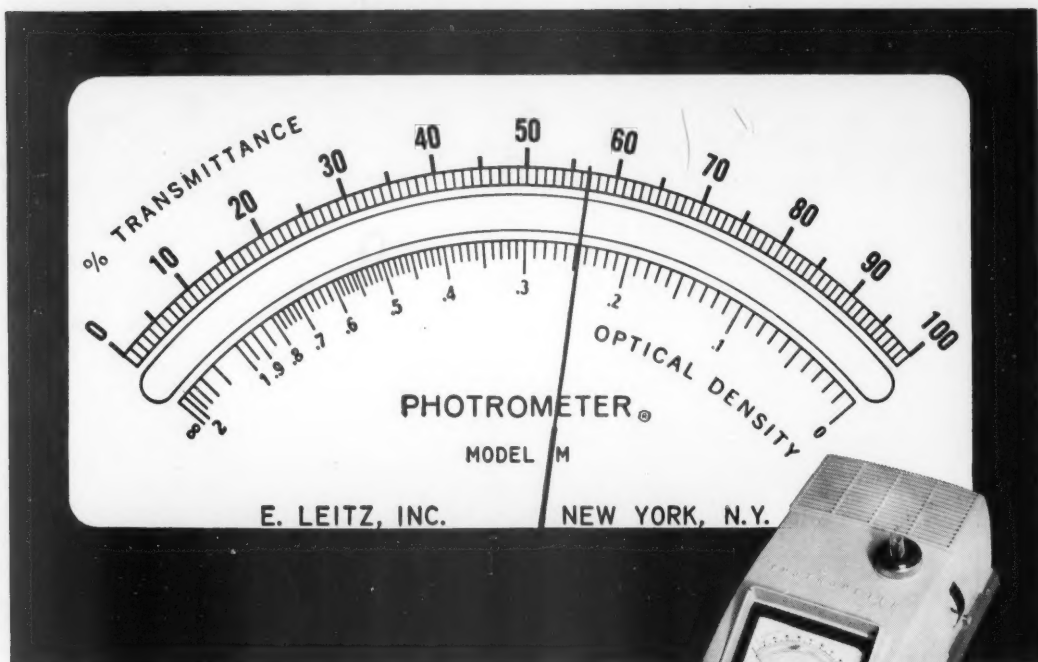
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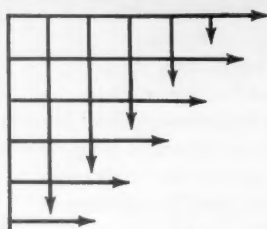
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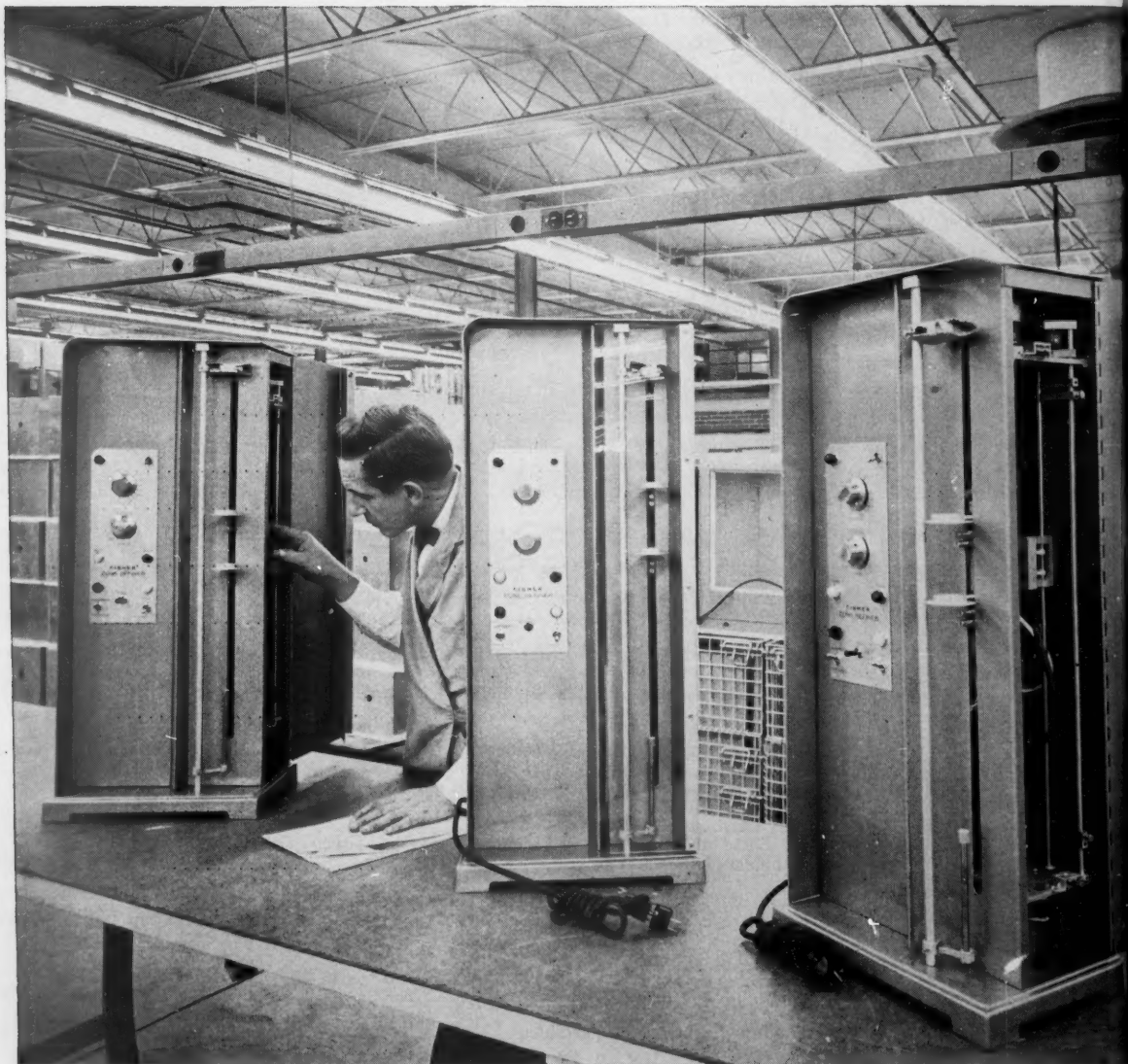
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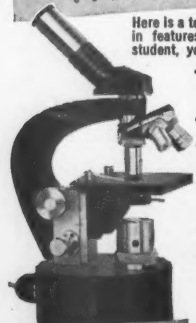
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Letters

Criteria for Research Grants

Where large sums are dispensed for research, selection of a basis for judging applications becomes of the utmost importance. Ernest M. Allen, chief, division of research grants, National Institutes of Health, is certainly to be commended for publishing these criteria, as applied by NIH [*Science* 132, 1532 (1960)].

Obviously, these criteria will be effective in eliminating ill-considered, thoroughly weak applications. But how would the strong, unconventional approach fare—the application in support of research that breaks away from precedents to blaze new paths?

To answer this question, it may be of interest to examine how some of the research projects of the past, which are today considered milestones of medical progress, would have fared had they been submitted to a National Institutes of Health of their respective times and judged by the accepted authorities of their day, organized as study committees and judging the applications by the criteria published by Allen.

To take a few examples: If William Harvey, whose brilliant studies led to the understanding of blood circulation, had applied to an NIH of his time for a grant to explore this subject, it would no doubt have been rejected under Allen's shortcoming No. 3 ("The problem is more complex than the investigator appears to realize").

Prior to the work of Albert von Haller, it was believed that the nerves were tubes which pumped "nerve fluid" into the muscles, thereby causing them to bulge and contract. Von Haller disproved this and introduced the modern concept of irritability and response to stimuli. An application for support from von Haller to an NIH of his time would apparently have been rejected under Allen's shortcoming No. 21 ("The investigator is spreading himself too thin; he will be more productive if he concentrates on fewer projects"), for von Haller was ranging widely between poetry and plant physiology.

Any support for William Beaumont's pioneering studies on gastric function would have been precluded under shortcomings Nos. 13 and 15 ("Controls are either inadequately conceived or inadequately described," and, "The number of observations is unsuitable"), for Beaumont worked with a single subject, a fur trader who had a permanent opening in his stomach as a result of an accident with a musket.

If A. L. Lavoisier had applied for a

grant from NIH to extend his quantitative combustion studies to human metabolism, he would have been turned down under shortcoming No. 24 ("It appears that other responsibilities would prevent devotion of sufficient time and attention to this research"), for Lavoisier earned his living as a tax collector.

If Louis Pasteur had applied for a grant to an NIH for support for his work on bacterial vaccines, he would have been turned down under shortcoming No. 17 ("The investigator does not have adequate experience or training... for this research"), for he was a chemist and had no training in medicine or physiology.

The criteria now being applied in the National Institutes of Health, according to Allen, would have resulted in refusal to support those investigations which became milestones of progress in medicine.

Is this the kind of thinking that should guide us today?

JOHAN BJORKSTEN

American Institute of Chemists,
New York, New York

The Author as Indexer

As a newcomer to specialized fields of information handling, I certainly profited from Helen L. Brownson's comprehensive summary, "Research on handling scientific information" [*Science* 132, 1922 (1960)]. The amount of effort going into development of systems for indexing documents through text analysis is impressive. Many of the systems are to be fully automated, the need for human judgments thus being eliminated.

Inclusive as the summary was, one very important aspect does appear to have been overlooked—namely, the author's role. Since the greatest authority on any item of literature is the author, is he not the one best able to classify the item properly? Would it not also simplify the whole matter of information handling if each author provided the necessary index terms with his manuscript? I am sure an author would readily accept this slight extra burden in order to make certain that the fruit of his labor attains its maximum usefulness.

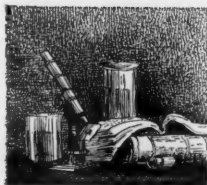
For classification to be performed by the author, only the development of suitable standard systems of indexing would be required. From standard instructions the author could easily supply the index terms directly in coded form, providing further simplification.

JOHN R. CLARK

Sandy Hook Marine Laboratory,
Highlands, New Jersey

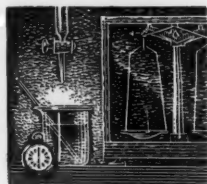
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a glance at yesterday in relation to today



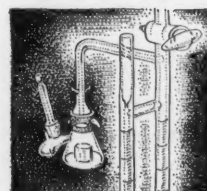
IN APRIL—(1799)—Medical and Physical Journal (London) reviews¹ an essay by Citizen Fourcroy on a newly discovered and controversial substance called “oxygen”—the very name of which, he feels, will draw upon him “numerous groups of men, animated by different opinions and passions, but alike enemies to this [concept].” Fourcroy believes that the animal system may be impaired either by excess or deficiency of this important vivifying principle. Its use, either internally or externally in particular diseases excites the “action of life”. Therefore, remedies may be classified as oxygenating or deoxygenating. The former increase the activity of the whole system, heat, circulation, force, and motion; the latter, on the contrary, diminish all these natural effects.

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IN APRIL—(1925)—Harvard investigators report² their estimations of the minimum molecular weight of 14 proteins. They point out, however, that present analytical techniques do not permit placing too great confidence in any single set of determinations. In some instances (e.g., the histidine and the tryptophane content of casein) different procedures have yielded significantly different results. “Only when different methods have led different investigators to essentially the same conclusion can we proceed to the furthest implications of the result.”

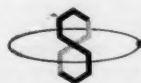
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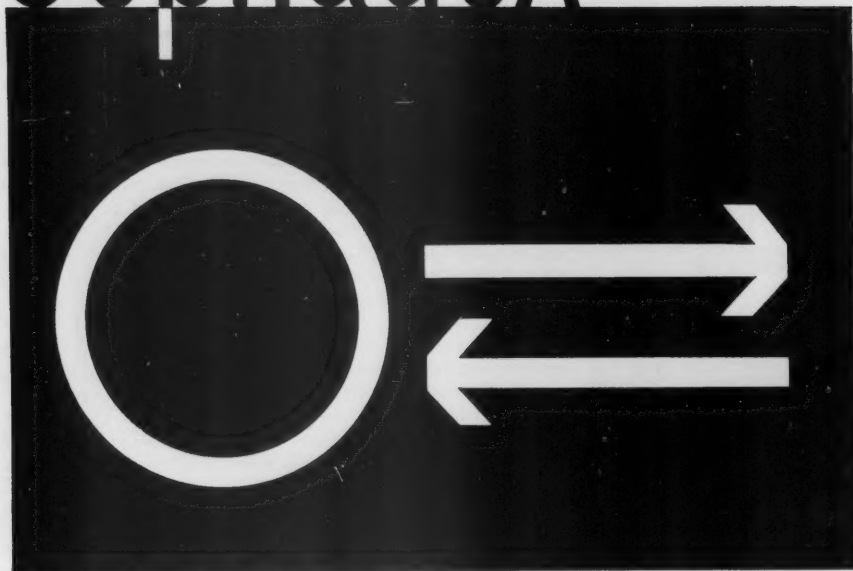
¹ Review: On the application of pneumatic chemistry to the cure of diseases. Med. and Phy. J. 1:145 (Apr.) 1799.
² Cohn, E. J.; Hendry, J. L., and Prentiss, A. M.: Studies in the physical chemistry of the proteins. V. The molecular weights of the proteins. Part 1. The minimal molecular weight of certain proteins. J. Biol. Chem. 63:721 (Apr.) 1925. 3. Wiebelhaus, V. D., and Lardy, H. A.: Phosphorylation of hexoses by brain hexokinases. Arch. Biochem. 21:321 (Apr.) 1949.



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Equal but Separate

President Kennedy's program of federal aid to education, including a bill granting almost \$2.3 billion to the states over three years for public school construction or teachers' salaries or both, poses the problem of how many good things the Administration can do at one time. Were the bill to include a provision barring funds from schools practicing racial discrimination, federal aid to education could be used to help enforce the Supreme Court's desegregation decree of 1955. But the bill must first get through Congress, and since such a provision would effectively kill the bill, it has not been included. The number of good things that can be done at one time is limited, but the Administration's course of action does make a little work for its conscience and for the consciences of all persons who advocate both federal aid to education and racial integration.

One of the bitter truths about education is that opportunities are not equal for all students. Difference in level of income is a familiar source of inequality. Parents with the necessary money have the option of sending their children to private schools. They also have the option of choosing one public school over another by the simple expedient of moving to the school district served by the better school. At the college level, the student simply by attendance receives a special kind of subsidy, since tuition even at private colleges generally does not cover full costs to the institution. These examples of inequality in opportunity resulting from differences in income are not offered as an argument that we must accordingly suffer inequalities to result from differences in race, but simply as a reminder that we live in an imperfect world.

In an imperfect world, of course, the way to get things done is to force one's opponents to accept something about which they are unenthusiastic as the price for something about which they feel strongly. This procedure is sound enough, and it would be nice if federal aid to education could be made to carry a civil rights burden. Unfortunately, pragmatism cuts both ways, and in the present case it is those who favor both federal aid and integration who face an unpleasant choice. They must choose between no federal aid or federal aid with some of it going to segregated schools. The reason is simply that the liberal Southerners in Congress, whose votes the Administration needs, dislike civil rights more than they favor federal aid to education. In fact, an amendment barring assistance to segregated schools, to be introduced while the conservative Southerners tactfully wait outside, is one of the tactics to defeat the bill promised by its opponents.

The deficiencies in education in the United States are serious in the extreme. In the matter of public school construction alone, the U.S. Office of Education puts the need at around 140,000 new classrooms, with no expectation that the property tax, the present mainstay of school financing, can even begin to meet this need. In the alternatives of no federal aid or federal aid with some of it going to racially segregated schools, the choice must be for the first alternative. Desegregation in this context is a side issue. To say this, however, is not to deny that the issue of civil rights is equally important, but simply to recognize that it must be dealt with separately. And balm for governmental and private consciences is available in the form of a more vigorous pursuit of desegregation by other means.—J.T.



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CURRENT PROBLEMS IN RESEARCH

Interior of the Moon

Observations from space vehicles will provide further clues to the history of the earth-moon system.

Gordon J. F. MacDonald

Study of the moon's surface has produced a wealth of observational material. Despite the abundance of observations, the origin of many of the surface features remains in doubt. By contrast, very few data relate to the nature of the moon's interior. Because of the inaccessibility of the moon's interior it is unlikely that any detailed picture of its nature will be forthcoming in the near future. The study of the lunar interior offers a wide field for speculation.

Astronomical Data

The mean density of the moon is well established at 3.34. This value is tantalizingly close to the density of a large number of silicate materials found on or near the surface of the earth. The densities of peridotite and eclogite, two rocks that may form portions of the upper mantle of the earth, are about 3.3. Indeed, Bullen (1) has reversed the argument and uses the mean density of the moon as evidence for a density of 3.3 in the upper part of the mantle.

While the mean density of the moon is well established, the distribution of density within the moon is as yet not known. It is generally assumed that the moon is a homogeneous body in which

density increases only through an increase in pressure. Jeffreys (2) assumes that the moon is of one material, with a density ranging from 3.28 near the surface to 3.41 at the center. The justification for this assumption lies in the apparent homogeneity of the earth's mantle over the pressure range attained within the body of the moon. In making this assumption Jeffreys ignores the inhomogeneous nature of the outer part of the earth and the possibility that the crust-mantle boundary may be a phase change.

It is possible to obtain an estimate of the density distribution from an analysis of the moon's motion about the earth and the rotation of the moon. The motion of the moon is complicated by the fact that the moon's three moments of inertia are different. On the average, the moon rotates at such a rate as to keep the same face toward the earth. The largest moment of inertia is about the axis of rotation, and we denote it by C . The least moment of inertia, A , is about the axis pointing towards the earth. The earth's attraction maintains a permanent tide within the moon, and this tide is along the axis of A . The principal moment, B , is along the tangent to the orbit. The differences between the moments of inertia give rise to observable peculiarities in the moon's motion. The study of these peculiarities is difficult because of the smallness in the differences in

the moments of inertia. A further difficulty results from the small ellipticity of the visible disk of the moon and the large irregularities of the lunar topography.

The triaxial figure of the moon causes the axis of least moment of inertia to perform small oscillations in both directions about the line of centers connecting the earth and moon. The moon's orbit changes because of the action of the sun, and as a result the actual motion is very complicated. The mean position of the moon's axis of rotation lies almost in the plane containing the pole to the ecliptic and the pole to the moon's orbit. The moon's axis of rotation oscillates about this mean position. The mean position of the axis of rotation is inclined to the pole of the orbit. This inclination depends on the ratio

$$\beta = \frac{C-A}{B} \approx \frac{C-A}{C} \quad (1)$$

Since the direction of the axis of rotation is well observed, this ratio is accurately determined.

A measure of the homogeneity of the moon is provided by the ratio of the moment of inertia C to MR^2

$$g = \frac{3}{2} \frac{C}{MR^2} \quad (2)$$

where M is the mass of the moon and R is the mean lunar radius. If the moon were a homogeneous sphere this ratio should be 0.6. For the earth, with its density concentrated towards the center, the value of g is 0.49. For a hollow sphere, g should be unity.

The effects of $C-A$ and $B-A$ on the orbital motion depend on their ratios to Ma^2 . The effects on the rotation depend on the ratio of the differences in moments of inertia to the moment C . Combining orbital data and observations of the rotation makes it possible to obtain g , and thus a measure of the density distribution of the moon.

The ratio of $C-A$ to Ma^2 is determined by the mean motion of the perigee and node. In order to obtain

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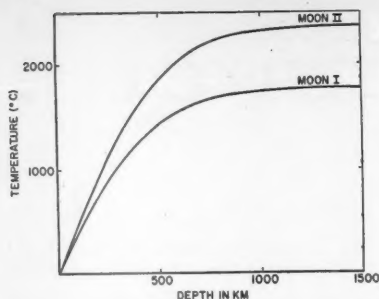


Fig. 1. Temperature distribution in the moon, after 4.5×10^9 years, for a cold moon (I) and a hot moon (II).

the effect of the figure of the moon, it is necessary to calculate the mean motion; in the calculations the moon is assumed to be spherical. In these calculations it is also assumed that the earth is a spherical body. The difference between the observed and the theoretical values then must be due to the effects of the figures of the earth and moon on the moon's motion. In a year the perigee moves by about 1.46×10^2 seconds of arc. Of this total motion, the figure of the earth contributes 6 seconds, while that of the moon contributes only 1 second. Recent satellite data establish a definitive value for the figure of the earth. In order that the effect of the figure of the moon can be abstracted from the observations, it is necessary to know the principal terms to at least one part in 10^6 . The principal term in the motion of the perigee is due to the sun.

The principal solar terms are calculated from a theory of the moon's motion developed by Brown (3). It now appears that calculations based on Brown's theory are not sufficiently accurate to determine the principal solar terms to the accuracy needed for the separation of the effect of the moon's figure. If Brown's theory is taken at face value and new data are used for the figure of the earth, the data on the motion of the moon, together with the inclination of the axis of rotation, give

$$g = 0.87 \quad (3)$$

This implies that the interior of the moon is considerably less dense than the outer parts. Indeed, it would seem that the moon is more like a hollow sphere than like a homogeneous sphere. This suggests very strongly that there are inconsistencies either in the reduction of observations of the moon's mo-

tion or in the numerical development of Brown's theory.

The physical librations of the moon provide an estimate of the ratios of the difference in moments of inertia to the mean moment of inertia. The physical librations are distinct from the geometrical librations. The physical librations result from the nodding of the axis of least moment of inertia about the line of centers. They are measured by obtaining the angular distance from a crater to a point on the limb. Since the limb is indistinct, due to the topography, these measurements have in the past led to inconsistent results. In recent years, photographic methods have been applied to the determination of the physical librations. A reduction of the values given by the Russian astronomer Habibullin gives results as follows:

$$\begin{aligned} \alpha_0 / \alpha_T &= 40 \\ \beta_0 / \beta_T &= 16.8 \\ \gamma_0 / \gamma_T &= 9.0 \end{aligned}$$

The outstanding feature of these results is that the observed ratios α_0 , β_0 , and γ_0 , where

$$\alpha = \frac{C-B}{A}, \quad \beta = \frac{C-A}{B}, \quad \gamma = \frac{D-A}{C}$$

are much larger than the ratios (α_T , β_T , and γ_T) that would be predicted for a homogeneous moon in hydrostatic equilibrium. The deviations between the observed and the theoretical values would be even greater if the moon were heterogeneous, with density concentrated towards the interior.

The observed values of α , β and γ indicate that the moon is far from being an equilibrium figure. This, in turn, implies that the interior of the moon must be able to support stresses of considerable magnitude. Rough estimates of those stress differences

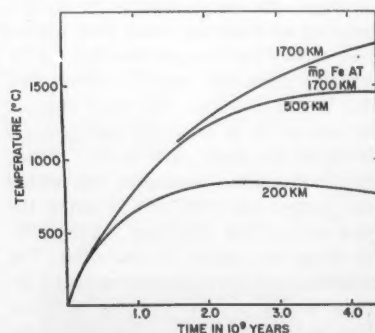


Fig. 2. Development of temperature with time at various depths for a cold moon.

created by the inequalities of the figure are of the order of 10 to 100 bars (2). Thus, the astronomical data on the rotation of the moon suggest that the moon is a relatively strong body capable of supporting strength differences comparable in magnitude to those supported within the earth (4).

The Thermal State of the Moon

The thermal state of the moon's interior is determined by the distribution of radioactivity, the distribution of thermal conductivity, and the temperature distribution at the time the moon was formed. Of these parameters, the two for which uncertainty is greatest are the initial temperature of formation and the radioactivity. The factor of uncertainty for thermal conductivity is probably about 2. In addition, the mechanism by which energy is transferred is not certain. Both convection and radiation may contribute to the transport of energy.

In 1959 and 1960 I carried out calculations on the thermal state of the moon's interior, assuming that energy is transported by ordinary thermal conduction and by radiation (5). In these calculations I assumed that the moon has the bulk composition of chondritic meteorites. My principal reasons for assuming a chondritic composition are reviewed in (6). The findings in support of a chondritic composition include the general agreement between abundances of the elements in chondrites and in the sun. Furthermore, the density of chondritic meteorites does not greatly differ from the mean density of the moon. The principal heat-producing elements in chondritic meteorites are potassium, uranium, and thorium, and the contents are 8.0×10^{-4} , 1.1×10^{-6} , and 4.4×10^{-8} g/g, respectively.

Figure 1 illustrates the temperature distribution that might be expected in a moon composed of chondritic material. In this model it is assumed that the radioactivity is uniformly distributed. Moon model I represents a cold moon. The initial temperature is taken as 0°C . The opacity is taken at the relatively low value of 100 cm^{-1} , and, therefore, radiation makes a noticeable contribution to the transfer of energy. Moon model II (Fig. 1) represents the present-day distribution of temperature that would be expected for a moon that had formed 4.5×10^9 years ago with initial temperature of 600°C and with

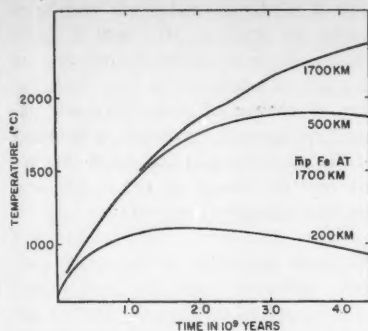


Fig. 3. Development of temperature with time at various depths for a hot moon.

an opacity of 1000 cm^{-1} . The central temperatures reached in the cold and warm moons are 1800°C and 2400°C , respectively.

Figure 2 illustrates the development of the temperature distribution within a cold moon as a function of time. It may be seen that after 3 billion years any iron present would begin to melt at a depth of 1700 kilometers. At this time there would be a tendency towards differentiation if a metallic phase were present within the moon. Figure 3 gives the development in time of the temperature distribution in a warm moon. The principal difference in models I and II is that the melting point of iron is exceeded at a depth of 1700 kilometers after 1.6×10^9 years, and at 500 kilometers shortly thereafter, in model II. At present, the outer 500 kilometers of a warm moon are cooling off while the inner 1200 kilometers of the moon continue to warm up.

A number of other models of homogeneous moons have been investigated. The results are summarized in Table 1. The surface heat flow for a moon of chondritic composition ranges from 10.3 to 16.4 ergs per square centimeter per second. The higher heat flows are

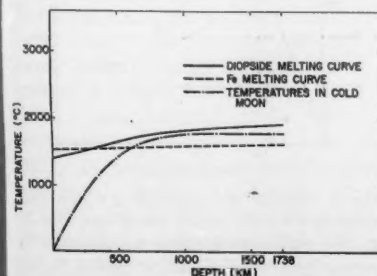


Fig. 4. Melting point of diopside (10) and iron (11) as a function of depth within the moon.

associated with the higher temperatures and lower opacities. If the moon is initially at 1200°C and there is no radioactivity, then the surface heat flow is 4.2 ergs per square centimeter per second at the present time. Thus, the initial temperature of around 1200°C would contribute about 25 percent of the present surface heat flow.

The outstanding feature of the temperature-depth curves for the moon is the shallow depth at which melting points of various materials are reached or exceeded. Since the moon is a relatively small body, the central pressure is low, of the order of 46,000 atmospheres. The low central pressure would not markedly raise the melting points of possible constituents. The thermal conductivity is sufficiently low so that only the outer portions of the moon are cooling to any extent. A combination of these two conditions results in a close approach of the melting-point curve and the calculated temperature distribution, as is illustrated in Fig. 4. The temperatures of the cold moon are plotted, as are the melting points of the silicate, diopside, and metallic iron. The melting point of iron is exceeded at all depths greater than 500 kilometers. The melting point of diopside is not exceeded, though the temperature closely approaches the melting point at depths of the order of 800 kilometers. Thus, in a homogeneous moon having a chondritic composition, the melting point of silicate materials is very nearly reached, even though the initial temperature may have been as low as 0°C .

It would thus appear that in a homogeneous moon the melting temperature of silicates is approached or exceeded, provided that the moon has the composition of chondritic meteorites. If the radioactivity is reduced by a factor of 2, then the temperature of melting is approached or exceeded if the initial temperature is greater than about 1000°C .

The astronomical evidence suggests that the moon is a relatively strong, rigid body. A strength of 100 bars implies that no major portion of the moon is molten. The discrepancy between the suggestions derived from the astronomical data and from the thermal models can be partially resolved if it is assumed that the radioactivity of the moon is appreciably less than that of chondritic meteorites, or that the radioactivity is concentrated towards the surface. A concentration of radio-

Table 1. Results of investigations of various models of homogeneous moons.

Opacity (cm^{-1})	Initial temp. ($^\circ\text{C}$)	Present central temp. ($^\circ\text{C}$)	Surface heat flow ($\text{erg/cm}^2 \text{ sec}$)
100	0	1780	10.3
1000	600	2380	12.4
1000	1200	2980	14.6
10	1200	2700	16.4
10	1200	1160	4.2

(No radioactivity)

activity towards the surface in turn implies a differentiated character for the moon.

It appears likely that even if the moon were chemically homogeneous the density distribution would undergo discontinuities. At the pressures and temperatures reached within the moon, several of the common silicate phases undergo transitions from low-density to high-density forms. Figure 5 illustrates the depth at which these transitions might be expected if the moon were initially cold (0°C) and homogeneous. Albite plus nepheline would transform to jadeite at a depth of some 750 kilometers, while enstatite would break down to pyrope, sapphirine, and sillimanite at a depth of around 500 kilometers. If the initial temperature were higher, the depth to the discontinuity would be greater. In a cold moon containing material of basaltic composition, the silicate phases would undergo transitions from the low-density to the high-density forms at depths between 500 and 1000 kilometers. If the moon were made up of chondritic materials the same transitions would take place. The density discontinuity in a material of chondritic composition would be a few percent because of the low alkali and alumina content of chondrites.

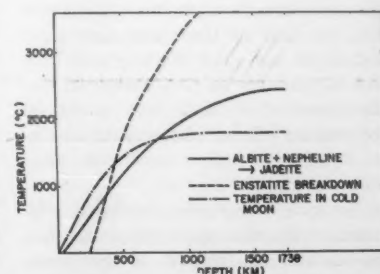


Fig. 5. Possible phase transitions within the moon. The solid curve is derived from data of Robertson *et al.* (12). The enstatite breakdown curve is taken from Boyd and England (13).

The thermal histories of the homogeneous models of the moon show that at present the outer parts of the moon are cooling while the inner regions are heating up. Because of the finite thermal expansion of the material making up the moon, this differential cooling and heating will generate thermal stresses within the moon. The build-up and release of these stresses provide a source of seismic activity. An important question for the exploration of the moon is the extent of such seismic activity.

As the temperature distribution within the moon changes, the dimensions of the moon must also change. During periods in which the moon as a whole is heating, the radius increases. If at present the moon is cooling, then the radius should be decreasing.

A study of the surface features of the moon may give some indication as to the thermal history of the moon, by limiting possible changes in the lunar radius. If the volume of the moon has undergone marked changes since the time of formation of the surface features, then the surface features should have undergone visible displacements. Large-scale strike-slip faults on the lunar surface are far more easily recognized than terrestrial strike-slip faults. The lunar surface is free of masking sediments and oceans. Furthermore, the complicated character of the lunar surface provides an abundance of land marks for the detection of relative horizontal movement. The veritable lacework of craters that forms the lunar surface provides an ideal reference against which horizontal movements can be detected. A close examination of the surface of the moon reveals that none of the craters have undergone displacements in which one side of a crater has moved relative to the other side. In a few cases it appears that one side of the crater may have undergone a vertical displacement relative to the other side. A horizontal displacement of half a mile could be detected on a lunar photograph; no displacements of this magnitude have been noted.

The lack of features associated with faults implies that the volume, and thus the surface dimensions, of the moon have remained more or less constant. If the circumference of the moon has been increasing, then we should expect normal faulting and the formation of grabens or rifts. If the circumference

of the moon's surface is decreasing, then strike-slip faults and thrust faults would be expected from the resulting compression. A decrease of 1 kilometer in the radius of the moon would result in a decrease in the lunar surface area of about one-tenth percent. The accompanying distortion of the surface features should be noticeable, particularly since it would be expected that the inhomogeneous nature of the lunar surface would lead to local concentration of stresses.

For a spherically symmetric body in which heat is produced at a rate A per unit volume, the equations of conservation of mass and energy combine to give the rate of change of the outer radius as

$$\frac{dR}{dt} = \frac{\alpha}{\rho_s C_p} \left[K \frac{\partial T}{\partial r} \right]_R + \frac{1}{R^2} \int_0^R \rho A r^2 dr \quad (4)$$

where α is the mean thermal expansion, ρ_s is the mean surface density, C_p is mean heat capacity, and K is the thermal conductivity of the surface. The rate of change of radius is proportional to the difference at which heat is flowing from the surface

$$-K \frac{\partial T}{\partial r} \Big|_R$$

(K is the thermal conductivity), and the rate at which heat is being produced within the body. If the heat flowing through the outer surface is equal to the rate at which heat is produced within the body, then the radius of the body remains constant. A change in radius can come about only through an excess of heat production or an excess of heat loss.

A number of factors are important in determining the difference between the rate of heat production and the rate of heat loss. If the radioactivity is concentrated near the surface, then the heat produced near the surface will reach equilibrium with the surface temperature in a shorter time than if the heat were distributed uniformly throughout the body. Of considerable importance is any initial heat that the body may have. This initial heat does not appear explicitly in Eq. 4 but does contribute to the surface heat flow. If a body had no radioactivity, then the initial heat would lead to a decrease in radius with time, since there would be a surface heat flow determined by the initial heat of the body.

Thermal calculations described in the previous section can be used to determine the rate of change of radius. In

these calculations the thermal expansion of the lunar matter has been arbitrarily set at 1×10^{-5} deg/ $^{\circ}\text{C}$. This value is likely to be low for silicates by as much as a factor of 2 to 3. Since the rate of change of radius depends linearly on thermal expansion, a doubling of the mean thermal expansion doubles the rate of change of the radius and the total change of the radius.

Figure 6 shows the radius and change of the radius of the moon with time, provided that the moon was initially at 0°C throughout. During the first 2×10^9 years the radius increased by about 5 kilometers in response to the high initial rate of radioactive disintegration. After that period of time the rate of increase of the radius decreases, but the radius reaches a maximum at about 4×10^9 years after initial formation. At present the radius would be decreasing, but at a low rate. The striking feature of the curve is the near constancy of the radius over the past 1.5×10^9 years. The size of the moon determines its thermal time constant, and it appears that the time constant for the change in radius of a homogeneous moon is about 2 to 3×10^9 years.

The case of an initially warm moon is shown in Fig. 7. The general features of the curve are similar to those in the cases discussed above and indicate that the rate of change of radius over the past few hundred million years has been very small.

Further models have been studied. The general features of the models are the same. The amplitude of the variation in radius depends on the initial temperature (lower initial temperatures give rise to the higher increase in

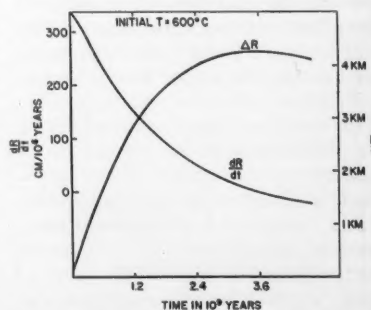


Fig. 6. Change of radius of a moon initially at 0°C , 4.5×10^9 years ago. Opacity, 100 cm^{-1} ; ordinary lattice conductivity, 0.025 joule per gram per second per degree centigrade. Final central temperature and surface heat flow, 1780°C and 10.3 ergs per square centimeter per second, respectively.

radius) and on the mechanism of heat transport. If the heat is transported by radiation or by any other mechanism in which heat is more efficiently transferred than by ordinary conduction, then the rate of change of radius is less over any interval in time and the total change in radius over a period of time is proportionately less.

The present surface features indicate that the radius of the moon has remained constant since their formation. On the assumption that the lunar surface formed at an early stage of the moon's history, such an observation could be explained by a number of hypotheses.

1) The radioactivity of the moon is less than that of chondritic materials. A lower radioactivity is also suggested by the close approach of the melting point and of the actual temperature gradient. If the initial rate of heat production is sufficiently small and the moon formed at a low initial temperature, then both terms on the right-hand side of Eq. 4 would be small and the corresponding change in radius would be small.

2) The radioactivity of the moon could be that of chondritic meteorites buried at a sufficient depth. The moon could have a low initial temperature of the order of 1500°C . The history of the radius in time would then be given by Figs. 6 and 7. Such a model for the moon would imply an age for the surface features of at least 2×10^9 years.

3) The moon is a chemically differentiated body with the radioactivity concentrated near the surface. In this case the temperature at depth might again be well below the melting temperature at all points. Furthermore, the rate of heat flux would be equal to the rate of heat production, and the surface heat flow would be due primarily to the initial heat possessed by the moon. Such a model of the thermal structure of the moon explains the lack of large-scale faults and the absence of abundant volcanic activity on the moon. The principal difficulty in such a model is the difficulty of providing a history for the differentiation of the lunar material.

In the models studied the outer portions of the moon are cooling while the inner portions are heating. There is a build-up of stress differences within the moon. If these stress differences exceed some critical value the stresses are relieved either by fracture or by flow. The rate at which the strain energy due to thermal stresses is re-

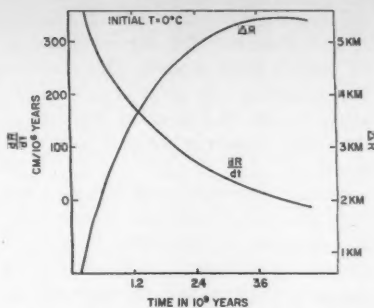


Fig. 7. Change of radius of a moon initially at 600°C . Opacity, 1000 cm^{-1} . Final central temperature and surface heat flow, 2380°C and 12.4 ergs per square centimeter per second, respectively.

leased can be calculated if a critical stress is assumed. For a strength of 100 bars the maximum strain energy per unit volume is 1.4×10^8 ergs per cubic centimeter. The models give a rate of build-up of maximum stress differences of the order of 10 bars per 10^9 years. The corresponding rate of release of strain energy by failure at 100 bars maximum stress difference will be 4×10^{21} ergs per year. This rate of release of strain energy is of the same magnitude as the present rate of release of strain energy on the earth, as measured by the intensity of earthquakes. If the moon has a chondritic composition, then the moon should have a high degree of seismic activity.

In the model studied, the greatest release of strain energy is at a depth of 100 to 700 kilometers. The assumption of deeply buried radioactivity implies deep foci for lunar seismic activity.

Dynamical History of the Moon

In a recent study (7), Munk and I reopen the question of the dynamical history of the earth-moon system and of the age of the earth-moon system. We have examined the astronomical data relating to the rate of change of kinetic energy of the earth-moon system. We find that dissipative processes remove energy from the mechanical motion at a rate of 3.2×10^{26} ergs per second. This figure is about three times greater than the figure obtained by Jeffreys (2). The discrepancy in the two estimates lies not in the data but in the method of reduction. It should also be noted that the rate of energy dissipated is somewhat greater than the present estimates of the rate of release of seismic energy in the earth.

The mechanism by which the energy is dissipated is still somewhat uncertain. Jeffreys argued that the energy was dissipated within the shallow seas. Munk and I, on reviewing the oceanographic evidence, demonstrated that the energy dissipated in the shallow seas is insufficient, by at least a factor of three, to account for the observed change in kinetic energy of the earth-moon system. A substantial portion of the energy may be dissipated within the body of the earth. This suggestion is strengthened by studies of the damping of seismic waves. Furthermore, recent analysis of bodily tide records in isolated continental stations suggests that the observed phase lag of these bodily tides is consistent with the interpretation that energy is dissipated within the body of the earth.

Extrapolation back in time of the present rate of dissipation is warranted only if the rate of energy dissipation has remained constant. The dissipative character of the earth's mantle depends only on the prevailing conditions of the temperature and pressure. The time constant for the change in temperature and pressure within the earth is very long, and it may be safely assumed that the earth now has much the same dissipative properties that it possessed a few billion years ago. The time needed for the moon to recede from a distance of 10^5 kilometers to its present distance from the earth is 1.3×10^9 years, provided our estimate (7) of energy dissipation is correct. This calculation does not take into account the nonlinear interactions as the moon moves closer to the earth. If the nonlinear terms are considered, the time needed for the moon to recede from a distance of 10^5 kilometers to its present distance would be a few hundred million years. The age of the earth is at least 4.5×10^9 years. The data on the secular acceleration of the moon therefore suggest that the earth-moon system is younger than the earth.

The arguments reviewed in the preceding paragraph reopen the possibility that the moon was captured by the earth at a late stage in its history. The problem of an orbital capture of the moon has been considered closed for a number of years, and a capture has been generally assumed to be extremely improbable. Recent work by Russian astronomers, stimulated largely by a remark of Schmidt's (8), reopens the question. Schmidt showed that the problem of capture is identical to the problem of breakup of double-star sys-

tems, provided that the direction of time in the equations is reversed. Since Schmidt made this suggestion, active work by a number of Russian astronomers (9) has done much to clarify the problem of capture. Direct numerical integration shows a possibility of capture, and general inequalities on initial conditions have been formulated indicating the conditions under which capture can take place. There has not been an application of these general results to the problem of the earth-moon system.

Observational Determination of the Nature of the Moon's Interior

A number of straightforward observations would do much to reduce the present uncertainty as to the nature of the moon's interior and the past history of the moon. The placing in orbit of a lunar orbiting satellite and the detailed trackings of the satellite would provide critical information on the ratio $C-A/Ma^2$, and this, combined with data on the inclination of the axis of rotation of the moon, would determine the mean moment of inertia. A knowledge of the mean moment of inertia fixes the degree of differentiation of

the moon and provides data of a fundamental character for the investigation of specific lunar models. This observation is perhaps the most critical of all, since it gives an immediate measure of the bulk properties of the lunar interior.

Seismic observations of various kinds will also yield valuable information. Measurement of the level of natural seismic disturbances will provide a means for estimating the current release of thermal strain energy. A network of seismic stations can be used to obtain a detailed description of the variation of elastic-wave velocity with depth.

The measurement of the surface heat flow involves the concurrent measurement of the near-surface temperature gradient and the thermal conductivity of the surface material. The surface heat flow can lead to estimates of the present thermal state of the moon. In combination with measurements of the radioactivity of the moon, measurement of the heat flow can provide theoretical limits for the initial thermal state of the moon.

The placing of a tidal gravimeter on the surface of the moon will permit measurement of the tides raised on the moon by the gravitational action of the

earth. In addition to the variation of gravity due to the direct actions of the earth (and of the sun), there is a variation resulting from the elastic distortion of the moon. The amplitude of this distortion determines the bulk elasticity of the moon, while the phase lag of the displacements fixes the anelastic properties of lunar matter.

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Eradication of Infectious Diseases

"Control" is an unending operation. After "eradication," no further effort is required.

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"Eradication" of infectious disease as a concept in public health has been advanced only within the past two decades, yet it is replacing "control" as an objective. The meaning of the term varies with the user, and the difficulties of achieving eradication, in any form, are usually underestimated. In this article (1) my own definition of eradication is offered, the difficulties common to all schemes of eradication are discussed, the significance of ani-

mal parasites in this connection is outlined, and brief comments are offered on selected eradication schemes.

Definition

In my definition, eradication is the extinction of the pathogen that causes the infectious disease in question; so long as a single member of the species survives, then eradication has not been

accomplished. The definition implies action on a world-wide scale, but world eradication has not yet been achieved for any infection. "Regional eradication" implies a basically unstable situation, because at any time the infection may be reintroduced by carriers or vectors from outside. The occurrence of occasional small episodes of infection in a cleared area does not invalidate the claim that regional eradication has been achieved in that area, provided the infection was imported. For areas where vectors are present but without the parasite, one may still claim eradication—as, for example, in Sardinia where there are anopheles without the *Plasmodium*, and in the United States where there are *Aedes aegypti* without the yellow fever virus. In South America, yellow fever virus cannot be eradicated, since it is endemic in the monkey population of the forest; however, eradication of the domestic vector *A. aegypti* from the continent is under way, and this situ-

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ation could be defined as "urban" eradication of yellow fever, and "regional" eradication of the mosquito.

Even if world-wide eradication of an infection is achieved, there is the possibility that a similar infection may evolve from related organisms still existing in nature after measures of eradication have been halted.

There is an essential difference between the concepts of eradication and control. Once eradication is achieved, the infection is gone forever, and the costly burden of recurring control measures may be dropped. Eradication can, therefore, be regarded as that state in which the infection does not return from infected areas after control measures have been abandoned. If procedures have to be continued to prevent return of the infection, then the state is one of control and not eradication.

Some pathogens persist in the body for long periods of time, and, strictly speaking, eradication has not been accomplished until the last parasite has died. However, in regional eradication, the practical definition can be used, and each infection can be judged independently. For example, in Brill's disease the rickettsiae persist in the body for very many years; in the United States, there must be people who became infected abroad and who are still carrying the pathogen, yet the infection must not be regarded as established here, since the chances of transmission are remote. Similarly, in malaria the parasite can persist in the body for years; many people in the United States are infected, but because the likelihood of transmission is very small, even without control measures, eradication can be claimed. The situation is different in an area where conditions favor the transmission of malaria; should eradication measures based on mosquito control be abandoned while the parasite still persists in the human host, then, even though the disease has not been reported for some time, there is a possibility of a recurrence of transmission, and the claim of eradication is not justified. In world eradication programs, the strictest adherence to the definition should be maintained; thus, in the case of smallpox virus, which can live for many months on infected clothing, a time allowance on this scale should be made after all other signs of the infection have disappeared. In malaria, before eradication as defined here can be claimed, there must be many years'

surveillance after the last case has been diagnosed.

The definition given above is in general agreement with the World Health Organization's definition for malaria eradication. In its original form the World Health Organization definition was interpreted (2) as meaning "the ending of the transmission of malaria and the elimination of the reservoir of infective cases in a campaign limited in time and carried to such a degree of perfection that, when it comes to an end, there is no resumption of transmission." The criteria of malaria eradication to be adopted included adequately demonstrated absence of transmission and endemicity for a period of at least three years, in at least the last two of which no specific general measures of anopheline control and no routine chemotherapy had been applied (3). The World Health Organization definition was modified still further to give more precision to the surveillance requirements (4), but it still does not go so far as to include the final elimination of the last parasite and does not mention related infections in animals or the theoretical possibility that the infection may evolve again.

History

Deliberate attempts to stamp out infectious diseases began in the closing years of the last century. In 1892, an animal infection, contagious pleuropneumonia of cattle, was declared eradicated from the United States after a campaign that lasted five years and cost nearly two million dollars (5). In England, in 1896, rabies was eradicated successfully by enforcing a muzzling order for all dogs for one year and enforcing a six months' quarantine for all dogs and cats. In 1917, the decision was made to eradicate bovine tuberculosis in the United States, under the Federal-State Cooperative Plan for Eradication of Bovine Tuberculosis. The program called for the testing of all cattle in the United States and the killing of the reactors, and it was extremely costly both in money and in animals. The campaign was not pushed to the extreme required for eradication, and it was unsuccessful in that bovine tuberculosis still exists in this country (5). Yellow fever was eliminated from Cuba in the first decade of this century by antimosquito measures, and this gave rise to such

high hopes that in 1914 Gorgas could state that world eradication of the disease not only was practical but could be achieved at a reasonable cost (6). With the discovery of forest yellow fever, these hopes were disappointed and the idea of eradication was discredited.

Modern ideas on eradication began with the work of Soper and his colleagues in South America. In 1930, some dangerous African mosquitoes, *Anopheles gambiae*, were discovered in Brazil by Shannon, and in a few years these had spread and were the vectors responsible for a disastrous epidemic of malaria in the northeast section of the country. A program to eradicate every single specimen was begun in 1939, and by 1941 the task had been completed (7). Side by side with this program, the control of *Aedes aegypti* mosquitoes had progressed so well that in 1942 Soper was encouraged to propose eradication instead of control. The following year, Bolivia was the first country to proclaim that this goal had been reached (6). Since that time the countries of South America have joined forces, aiming for complete continental eradication. By 1959, substantial areas had been cleared (8) (Fig. 1).

These successes with mosquito eradication made *eradication* a respectable term once more, so that world eradication of smallpox and malaria are now proclaimed aims of the World Health Organization, in programs supported by many countries and backed financially by the United States. At present, eradication is described as the aim in many other infectious-disease projects.

Basic Program Needs

All eradication programs have many needs in common. These include the need for political stability, for popular support, for adequate organization, for logistic and technical backing, and usually for an efficient quarantine system to prevent reinfection of the cleared area. Most important of all, the efforts must be pushed to the limit until the last parasite has been eliminated. The last 5 percent is as important as the first 95 percent. Anything less than 100 percent is not eradication.

Political stability. Eradication programs are usually long-term, often requiring international cooperation. Obviously, nations work together better

if they are at peace and friendly. Political upheaval and war usually disrupt such projects, and in countries like Tibet, where fighting is in progress, eradication programs are not likely to succeed. However, the recent collaboration of so many countries on issues such as malaria and smallpox has shown that much can be done even in a troubled world.

Popular support. Obviously, a program of eradication, with all its costs and inconvenience, will not be successful if it does not have popular support, even in a small country. On a world scale, this task of insuring popular support might well daunt the most fervid supporter of the principle were it not for the United Nations. It is only through the United Nations that the two programs of smallpox and malaria control have been adopted by the majority of people, and even then it is clear that some of the nations involved have only a lukewarm interest in the project, while mainland China, biggest of all countries, with its 600 million people, is not even in the United Nations.

Great difficulty arises in areas where an infection of global or continental significance is of no particular public health importance locally. It is difficult to persuade a community to put up the funds and make the effort required for something that causes little local inconvenience. For example, a few countries joined in malaria eradication only after some hesitation; for them, malaria was simply not a public health problem, and there was no public pressure to organize expensive measures to benefit neighboring countries.

The costly and time-consuming efforts made to eradicate *Aedes aegypti* mosquitoes in urban areas have been substantially successful in South America (8), but as there is no yellow fever in the United States, there is no public pressure to get rid of *Aedes aegypti* mosquitoes there (Fig. 1). None the less, the United States has an international obligation to eradicate this species of mosquito, for its representatives supported and voted for the resolution in the first meeting of the Directing Council of the Pan American Sanitary Organization, a meeting in which it was resolved that *Aedes aegypti* mosquitoes must be eradicated from the Americas (9). As long as there are *Aedes aegypti* mosquitoes in North America, there will always be a likelihood that they will reinfect the

areas in South America that have been cleared.

Syphilis might be eradicated from the United States by means of antibiotics and technical services already available, but it is unlikely that the public would accept an eradication program.

Technology. Eradication in any particular country may be impractical because the government lacks the funds or the personnel or the equipment or the organization. In certain nations of Africa, Southeast Asia, and other parts of the tropics, the number of physicians and other trained personnel may be too small even for routine tasks, let alone the difficult and burdensome techniques of eradication. When the total national budget is inadequate, the proportion allotted for health purposes is usually small.

Equipment may be scarce, not to mention spare parts and repair technicians. Transport is frequently difficult because of a scarcity of vehicles and drivers and even of passable roads. For eradication it is not enough to reach most places; one must reach all places. Usually 95 percent are reasonably accessible, but the remaining 5 percent are equally important.

The administrative organization of the national health department in the country undertaking eradication procedures must be strong enough to take the load. Usually, in underdeveloped countries, the department is so small that one man does work that should be done by ten. Frequently major duties are left to clerks, since no one else is available. To expect these overworked people to take on responsibility for a large additional program is to be overoptimistic.

It might be expected that foreign aid would supply the needed technicians, administrators, equipment, and supplies. This it can do to a large extent, but there is a crucial service that can be performed only by the host nation itself. For example, the first stages of a program are usually easy enough, with teams of workers, imported or trained by foreign technicians, spraying the countryside with insecticides, giving injections or vaccinations, or handing out pills, and with everyone pleased as the disease in question recedes. But when the foreign teams depart, the task of finishing the job and of continuing surveillance falls to the host government. Then the government needs an efficient health service, with trained doctors

who, in the course of their duties, will spot and report any recurrence of the disease. This program of surveillance has to be carried on for years in order that recurrences may be promptly discovered and stamped out in time. This task may be beyond the scope of any foreign aid, and all too often the national health department simply cannot carry it out. The final results over a ten-year period might well be especially disappointing if the program had started off well.

Reintroduction of a pathogen is an obvious danger where the operation is limited to a country or a continent, with infection remaining in regions outside. The usual method is to enforce quarantine measures, but the volume and nature of travel nowadays, especially by air, is making quarantine increasingly ineffective.

Biologic Factors in Eradication

On the basis of modern evolutionary theory it may be assumed that all human infections are derived from ancestral animal infections, since man himself was once a nonhuman animal. All human infections have related pathogens still existing in animal hosts, and the nature of these animal pathogens to a large extent decides whether or not an infection can be eradicated. Man belongs to the order Primates, and his relations the apes, the monkeys, and other primates share with him parasites that have been handed from one generation to another from their common primate ancestor. Elsewhere it has been suggested that these parasites include the intestinal protozoa, pinworms, herpes virus, malaria parasites, and so on (10, theory 2). In addition, there is a sharing of parasites among animals in intimate contact in the same ecology, as, for example, between man and his domestic animals. Sometimes this sharing is continued without change in the form of the parasite, and a new form of zoonoses is established, while in other instances a newly parasitized species of host will convey the parasite within its own population and in time a new strain will be selected that is largely specific to that host. Elsewhere it has been suggested that this is the way in which the pox viruses evolved among the animals brought together into man's ecology when man settled down and domesticated animals (10, theory 6).

Some of these relationships are close indeed; others are not so close, and some are fairly distant. When any eradication of an infection is contemplated, it is essential that the evolution of the agent be studied to determine the nature of these relationships and the effect they will have on the final result of the program. Related animal infections can be grouped as follows.

1) *Identical*. These infections are the zoonoses. From the point of view of eradication they can be subdivided into infections of wild animals and infections of domestic animals. If wild ani-

mals are involved (as in rabies, yellow fever, plague, rickettsial infections, or salmonella infections), then eradication will be difficult if not impossible. If only domestic animals are involved (as in *Mycobacterium bovis* infections, brucellosis, and glanders), then "regional" eradication is easy, for all that is necessary is to test the animals and kill the reactors, or else immunize the stock. However, research may show that most infections in domestic animals occur also in wild animals, and that world eradication may be impossible.

2) *Closely related*. In nature, closely

related species sharing the same ecologies compete with one another, and this must happen with parasites also. Possibly the distribution of each species is to a certain extent dependent on this interspecific competition. A zoonosis like yellow fever is related to a wide range of other arbor viruses and almost certainly is affected by them. This is the explanation sometimes proposed for the absence of yellow fever in India, where the facilities for spreading have existed for at least 2000 years. If yellow fever virus were completely eradicated from Africa, it might well



Fig. 1. Status of the *Aedes aegypti* eradication campaign in the Western Hemisphere in December 1960. "*Aedes aegypti* eradication completed" signifies that eradication has been verified in accordance with the standards established by the Pan American Sanitary Bureau. [Pan American Health Organization]

be that related, competing viruses would emerge prominently in that area.

Parasites similar to malaria parasites of man exist in apes and monkeys. The question as to whether they are identical is a matter of urgent research at the moment, but in any event there is no question but that man can be infected with these parasites (4). Should the human malaria parasites be eradicated but not the vectors, then, after the eradication measures had been halted, man would be reinfected from the primates, if these have identical parasites, or if they have not, over a period of decades human parasites might re-evolve from parasites of the primate reservoirs. In either case, human malaria would be likely to reappear.

As to treponemal infections, the various species are probably mere variants of one basic organism (17). Interspecific competition may partially determine whether a population contracts yaws or syphilis. Eradication of yaws will probably result in an increase in syphilis.

3) *Substantially different.* An infection such as smallpox is closely related to infections in other animals in man's immediate ecology—animals such as mice, cows, horses, sheep, or chickens. It is possible that all of these infections derive from a radiation of a single organism that occurred at the time man first settled down and domesticated animals (10, theory 6). These organisms are now so highly adapted to their hosts, and conditions have so changed from those under which they evolved, that the possibility that smallpox would re-evolve appears to be remote. The chances, therefore, of permanent eradication of the infection seem good.

4) *Very remote relationships.* Organisms like the leprosy bacillus have probably been symbiotes of man and his predecessors over many millions of years, are closely adapted to man, and have no close relations in other animals. Once eradicated, the chance of their re-evolving is extremely small.

It is becoming increasingly recognized that an organism that has radiated into many species is more capable biologically of surviving than one which has only a few species (12). A large organismal group is well equipped to withstand the adversities of changing environments and to adapt to new conditions as they arise. This strength arises from the variety of genetic mechanisms present in the radiation, in contrast to the limited range of mechanisms for organismal groups with only

a few species. In general, wide radiations are found mainly in the locations of origin of the ancestral organism, and only single species or narrow radiations are found in areas where the organism has been newly introduced, for it takes considerable time for new species to appear. Eradication procedures will therefore be easier to complete and more successful, in long-term effects, when employed against species of parasite or insect vector that have colonized the area in recent times than when employed against species that have been established there perhaps for millions of years.

The program to eradicate *Anopheles gambiae* in Brazil was a success, possibly because the mosquito was an introduced species, while a similar program against *A. labranchiae* in Sardinia was a failure in the sense that the mosquito species was not completely eliminated, because the anopheles in Sardinia were indigenous to the island and probably had been there many thousands or even millions of years (13). In addition to the mosquitoes which have become adapted to feeding on man within recent times, there was the original native stock, still feeding on wild animals. These mosquitoes of the original stock were not greatly affected by the eradication program and, presumably, form a reservoir from which fresh strains of domestic mosquitoes will evolve now that the program has terminated. Similarly, eradication of *Aedes aegypti* is proceeding very well in South America, where it probably is a newcomer of only some 400 years' standing, and where wild strains in the forest are as yet unknown. The story would be different should a similar program be attempted in East Africa, where wild strains are well established in the forest.

It is sometimes said that when an organism has been reduced to very small numbers it cannot survive and will die out spontaneously. This idea is of practical importance in eradication programs, for the last few sources of infection are difficult to reach. It is probably often true as applied to animals that are genetically diploid, but not necessarily so with microorganisms that are haploid. For example, the whooping cranes are probably doomed to extinction merely because there are only about 40 of them left alive. Deleterious or lethal mutations will occur occasionally in them; since most will be recessive, those that do not result in death will be stored away without

expressing themselves. The close inbreeding that occurs in so small a population as 40 will result in these recessive deleterious mutations becoming demonstrated in the phenotype, so that the birds will become increasingly unfit to survive. They will be saved only if the environment changes substantially in their favor.

With haploid organisms, this is not the case, for any mutation is likely to be expressed immediately in the phenotype, and if the mutation is sufficiently deleterious, the individual organism will fail to survive. The future population of the haploid organism will consist only of the descendants of those without the mutation, so that small numbers do not necessarily indicate that the population is doomed to become extinct.

In a vector-borne infection, the pathogen will die out if the density of the vector is too low. This is a well-recognized phenomenon in malaria, yellow fever, plague, and filaria, and usually in control programs there are indices, such as the *aegypti* or the *cheopis* indices, of the permissible levels of vector densities for control of the infections. Should the numbers of these vectors be kept permanently below the threshold levels, then in time the pathogens will be eradicated. However, in any large country there may be small local pockets where high density levels of the vectors may persist, even though the general level for the area is low, and in an eradication program these must be sought for diligently. These pockets will not be so important in an infection like yellow fever, where the infectious process in the host is brief and the host population soon becomes immune to the pathogen, but they can be extremely important in malaria and filaria, where the host can carry the parasites for years.

Certain infections have been known to dwindle to small numbers and then disappear spontaneously. The extinction, however, was not due to the parasite population's falling below a hypothetical numerical threshold but to the parasites' having lost their fitness to survive in the environment. "Fitness" can be defined as an organism's capacity to produce regularly as many viable members in one generation as in the preceding generation, for if it produces fewer in each succeeding generation it will become extinct. Changes in environment and in behavior in places such as England and the United States in the past hundred years have tipped the

balance against many parasites such as lice, the malaria parasite, the cholera vibrio, bubonic plague bacilli, and tubercle bacilli, and these infections, if they have not completely disappeared, are becoming less and less frequent. This process is clearly due to environmental changes and not to mere smallness in numbers of the parasites; the paucity of the organisms in the closing stages is merely the final step in a continuing process.

In a country where conditions favor the parasite, the elimination of this last trace of the infection can be extremely troublesome; yet until it has been accomplished, the campaign will not be a success. If the operating procedures are stopped prematurely, the infection will return, and either the program will have to be recommenced or else all the effort will have been wasted. In Ceylon, antimosquito measures were commenced in 1945 with the then newly available residual insecticide DDT, and the results exceeded expectations, for within one year there had been a dramatic fall in the incidence of malaria. After a while the general spraying was stopped because of the increasing resistance of the mosquitoes, and reliance was placed on a surveillance system, with spraying of local infected areas. However, the malaria did not dwindle and vanish as expected but continued, and at the end of ten years it was still present in certain small foci (14). Malaria had been controlled but not eradicated. More vigorous measures are now being taken to discover and deal with these small foci.

The story has been much the same in Haiti, where yaws eradication is being attempted (Fig. 2). There had been 45,356 cases of yaws reported in 1949 in the island; in 1950 the general population had been given penicillin, and in 1953 only about 400 cases of yaws could be found. Every year since then the program has continued, and the early eradication of yaws has been eagerly expected, but each year up to 1959 there continued to be a hard core of about 300 cases (8, 15). In nearby Jamaica, the yaws eradication program had made considerable progress when the teams for checking and surveillance were withdrawn prematurely. In 1959, 415 new cases of infectious yaws were reported, and the program is to be resumed (8).

This kind of experience underlines the difficulties in the later stages of an eradication program. Once the first enthusiasm for the program has dwindled

and the disease to a large extent has disappeared, it is difficult to keep the teams in the field and at a high level of efficiency. The mode of transmission may be difficult to see, so that cases pop up in unexpected places, and often supreme efforts are necessary to bring the transmitting agent to light. Soper has called this level of infectivity the "threshold of visibility" below which the mode of transmission of the infection cannot be seen with routine methods (16), and it is this that causes campaigns to drag on year after year when, according to all expectations, they should have been completed.

Eradication in Practice

Small islands are obviously the places where eradication efforts can best be made, for there the problems are clear-cut and quarantine measures are easiest to enforce. In England, several infections have been deliberately eliminated, including smallpox, rabies, and glanders, while typhus, plague, relapsing fever, malaria, cholera, and possibly leprosy have vanished, probably as a result of changing environments and habits. Smallpox was everywhere in England in the 18th century, but in 1867 vaccination was made compulsory.



Fig. 2. "Show your feet" is the order of the day in Haiti, where, with the assistance of the Pan American Sanitary Bureau and the United Nations International Children's Emergency Fund (UNICEF), the government is carrying out a program to eradicate yaws. Signs of the infection are frequently found on the feet. UNICEF contributes equipment and supplies, while technical advisory services are provided by the Pan American Sanitary Bureau, executive body of the Pan American Health Organization and regional office of the World Health Organization. [Pan American Health Organization]

By 1871 the annual death rate per million people was down to 1012, and in the ten-year period 1911-1920, not a single death was reported. However, a very mild form was common during the 1920's (17). Vaccination is no longer compulsory, and the immunity status of the nation is no longer so high, so that introduced infections every few years cause small outbreaks, but smallpox still is not an endemic disease.

Glanders in England was eliminated by slaughtering all horses with the infection.

There has been almost no plague in England since the 17th century, partially as a result of the change in the species of rats in the island, and partially because of the vigorous campaigns at ports to keep out foreign rats. However, in the early 1900's, sylvatic plague was discovered in East Anglia, where a handful of human cases was diagnosed, and this persisted for a few years until it died out spontaneously. Presumably it had been introduced at a nearby port.

Higher standards of living and greater cleanliness were responsible for the disappearance of typhus and relapsing fever, for body-lice infestations are uncommon, although infestation with head lice still is found. Cholera has not been seen since the 1860's as a consequence of improvements in sewage disposal and management of water supply. Malaria has disappeared, partially because of the draining of the marshes and partially because its foothold in the country was always precarious as a result of the low summer temperatures. Also, the vector mosquitoes prefer feeding on animals to feeding on human beings.

Ceylon is another island with a good record of eradication of infections. Within the past 20 years, smallpox, plague, and cholera have all been wiped out, although each is likely to be reintroduced from time to time from India, which is only 18 miles away, across the Palk Strait. Smallpox was dealt with by maintaining high levels of vaccination immunity. Cholera and plague were both introduced infections which responded well to orthodox public health measures. The plague-carrying fleas had been imported from India and were limited to the port area of Colombo and to one or two small sites on the coast; rat-control measures have caused the infection to die out (18).

As for eradication on a regional scale, in America north of Mexico, several

infections have disappeared. The last reported case of smallpox authenticated by isolation of the virus was in 1949 in Hidalgo County, Texas (19). Malaria dwindled with drainage of swamps and mosquito-proofing of homes. Control projects such as those of the Tennessee Valley Authority and the Malaria Control in War Areas were also effective, so that by the end of World War II the surprising discovery was made that, without widespread use of DDT, malaria as an indigenous infection had practically ceased to exist, although it is continually being imported (20).

Yellow fever was easily eradicated in the United States, once the mosquito vector had been identified, and so far it has not been reintroduced. The last cases of yellow fever were in New Orleans in 1905, when about 1000 deaths occurred (6). There has been no cholera for nearly 100 years.

Smallpox

Smallpox is the ideal target for an eradication program on a world scale. Since the layman, terrified by its threat, can see that it is infectious, control and eradication measures usually receive full backing, even in primitive areas. Vaccination gives a solid immunity for about three to five years and a modified immunity for life. The vaccine is easy to make on a mass scale, even under field conditions, and remains potent for seven to ten days, without refrigeration, in the "wet" form and for six months to a year in the "dry" form. Little in the way of highly skilled technical help is required, except for overall direction and evaluation, for the techniques of vaccination are simple (21) (Fig. 3). The chances of the infection's evolving again are small.

Malaria

Malaria has often been described as man's number one killer. The discovery of residual insecticides gave rise to the hope that at long last a way had been found to deal with the menace. The subsequent appearance of resistance to insecticides led to the belief that, if this new weapon was to be effective, it had to be used once and for all, before its edge was blunted by this resistance. The objective of world eradication has been proclaimed by the World Health Organization, supported by the United

States, and agreed to by many nations, and programs are now in progress in a number of countries. No one envisioned the task as being easy, but unexpected difficulties are arising. Where transport, communications, health services, and supplies are poor or ineffective, especially in the less developed areas, the campaigns suffer.

The practical difficulties of malaria eradication are so formidable that the time for completing the program with current weapons must be measured in decades rather than in years. At least 20 years will be required and perhaps many more.

This period will be shortened drastically only if research produces new and more efficient techniques of killing insects or eliminating plasmodia on a mass scale. In any country a minimum of ten years' surveillance is necessary to insure that the last parasite has been killed. This was illustrated recently in the United States when a small pocket of infection was found in Oklahoma, several years after the indigenous infection was supposed to have disappeared (22). If this can happen in the United States it is even more likely to occur in countries with primitive health services.

If and when the last plasmodium parasite in a human being has been killed, and eradication on a world scale has apparently been achieved, the next question will be how to deal with similar parasites in animals, particularly monkeys and apes. Elsewhere it has been proposed that human and simian malaria are variants of the one ancestral parasite (10), the ape and monkey plasmodia being closely related to, or even identical to, the human parasites. Recently, natural transmission of simian malaria to human beings has been reported (4), and this opens up the disturbing possibility that malaria is a zoonosis, somewhat like yellow fever. Obviously this matter needs further research. If a simian reservoir does indeed exist, then eradication of malaria as presently contemplated will not be possible.

Poliomyelitis

Eradication of poliomyelitis virus is also being discussed. Production of live attenuated virus for use as an immunizing agent gives some hope that, through oral vaccination of large numbers of individuals, the wild virulent strains



Fig. 3. Lady volunteers in Khulna, East Pakistan, trained in the technique of smallpox vaccination. In countries that have the purdah system, male technicians cannot vaccinate the women, and professional women health workers are very scarce.

will be replaced by harmless strains. What is being suggested is a practical test of a bitterly fought theoretical problem, known to biologists as Gause's principle or the "competitive exclusion" principle of Hardin (23). In its simplest form this can be stated as follows: "Two related species of the same ecology cannot live together in the same place," for one species will have an advantage over the other and in time will replace it. The question in poliomyelitis will be, which species will survive, the virulent wild virus or the vaccine? If it is proposed merely to release doses of the vaccine in the hope that it will spread under its own agency and replace the other virus, then the effort is almost certainly doomed to failure, for the wild strains have been selected under intensely competitive conditions over long periods and presumably are far better adapted to life under natural conditions than is any "hothouse" laboratory strain that is liberated. The all-important capacity to resist adverse circumstances while being transmitted from host to host in nature has been ignored during the passage procedures in the laboratory, for passive transfer by syringe or pipet is not likely to have encouraged the selection of strains resistant to adverse conditions outside the body. As a result, the vaccine virus

can be expected to have relatively little capacity to move to new hosts, as compared with the wild strains, and is unlikely to become established as a self-perpetuating organism. The experience of the Russians has shown that about 50 percent of protected persons excrete live vaccine within three to five months after vaccination (24), but in contrast it is well known that during epidemics of the wild strains, almost everyone in a small, intimate community is infected. Experience in the United States indicates that the vaccine virus spreads poorly and does not establish itself as a permanent infection (25). The differences in spread in the U.S.S.R. and in the United States may be related to variations in sanitary conditions.

Elsewhere it has been proposed that for every infection and set of circumstances there is a minimum host population that is necessary to support the infection on a permanent endemic basis (10). The fact that poliomyelitis infection dies out in small communities has been recognized (26). In a large human population, the number of individuals susceptible to the virulent poliomyelitis infection can be reduced below this threshold level by repeated feedings of the competing attenuated and immunizing live virus. When this threshold is passed, the virulent wild virus will

automatically die out. The percentage of susceptible individuals in the community that form this threshold population will vary from one population to another, being lower where the chance of person-to-person contact is high, as in areas with, say, 1000 persons per square mile, and high in areas with only five or ten persons per square mile. To state this another way, it may be necessary to immunize 90 percent of the people in a town and only 75 percent in a rural area to reach the threshold level at which the wild virus disappears.

In eradication programs confined to a continent, there will be no means of keeping out reinfesting imported strains, for there is no practical way of detecting carriers of poliovirus. This means that occasional cases of poliomyelitis will occur, but that, at the worst, any epidemic resulting will be small and sharply limited. It does not follow that, if the whole world were brought up to the required level of immunity and the wild strains of virulent virus became extinct, these strains would have been eradicated for good and all further efforts could be abandoned. The circumstances that led to the evolution of the wild strains will presumably still be operative, and natural selection would quickly produce new strains from the vaccine virus, so

that the immunizing procedures would have to be maintained indefinitely. By practical definition, this situation would be one of control and not eradication.

Cholera

Cholera as an endemic infection is now confined to small areas of South-east Asia, principally the Bengal area of India and East Pakistan. Elsewhere it has been suggested that the infection is basically a rural one and is due to the fact that the only sources of water in the dry hot months are the highly polluted "tanks" or ponds of surface water (27). If these tanks were replaced by water supplies from unpolluted sources, then there is a good possibility that cholera would disappear from the world. Of course, Bengal is not unique in having such a situation, and similar choleraic-disease-causing vibrios might evolve in pond water in other parts of the world. Such a situation seems to occur in Indonesia, where repeated outbreaks of "paracholera," due to a different vibrio, are reported. Steps are now being taken to provide the people of Bengal with clean water; if these are successful, cholera may well disappear completely, although paracholera may persist.

Discussion

Eradication has been demonstrated many times to be entirely practical within certain limits, even with the techniques of today. Modern research is proceeding so quickly that many tasks that now seem impossible or extremely tedious and time-consuming may tomorrow be quite simple and quite rapidly performed. Most of the practical difficulties listed earlier in this article may be resolved in one or two decades.

Presumably, there will be rapid improvement in such areas as transport, logistics, and the strengthening of health services. Tasks such as the inoculation of people by the tens of millions will be speeded up by machines such as the hypospray jet injector (28). The dosing of people with drugs through additions to food or drink will make mass chemotherapy a practical matter. The development of live vaccines that can be given orally to babies soon after birth may immunize the populations of the world against many viruses. Such techniques, which are emerging in the laboratory today, may be available for use in the field in the near future.

Therefore, we can look forward with confidence to a considerable degree of freedom from infectious diseases at a time not too far in the future. Indeed, if the present pace of research and the present increase in the world's wealth continue, and if we suffer no major calamities such as an atomic war or an uncontrolled population explosion, then it seems reasonable to anticipate that within some measurable time, such as 100 years, all the major infections will have disappeared. This desirable goal will not be easily reached, for the difficulties are many, and unpleasant surprises are inevitable. Most of all there must be very much more research. And even as we are successfully eliminating one set of infections, new ones will almost certainly appear, for we live in a world swarming with potential pathogens in many forms. Evolution is not merely something that happened in the past; it is an essential part of both the present and the future, so that out of all the microorganisms that are continually seeking to invade our bodies, one that is favored by changing conditions will occasionally succeed. Always we will have to be on our guard, watching for signs of danger among the potential pathogens and stamping out the

latest comer among them in the small focus in which it is evolving, and before it has the opportunity to spread across the world.

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On The Unity of the Sciences

Interactions among the physical and biological sciences show that unification is progressive.

Frank L. Horsfall, Jr.

It was only 16 years ago that the seeds were sown which led gradually to what is now so clearly a revolution in the biological sciences. In 1944 it was announced by Avery, MacLeod, and McCarty that nucleic acids may possess biological activity; that they can direct and orient inheritance in bacteria. This now classic paper created a storm of protest, and the conclusions were vigorously opposed by many reputable authorities. It was nearly eight years before the full significance of this astonishing discovery was generally recognized, and it took almost another eight years for the revolution it initiated to come into full flower. In the interval, several Nobel prizes were awarded, though not to the original discoverers, for remarkable advances in knowledge which were closely related either to nucleic acids or to their genetic activities.

This revolution in the life sciences has produced results almost as remarkable and as unexpected as those of the revolution in the physical sciences that was initiated by the discovery of radioactivity. The formal lines between the several disciplines have disappeared in biology just as they were broken down in the physical sciences. It is no more possible now to make a clear distinction among cytologists, geneticists, immunologists, and virologists than to make one among chemists, physical chemists, and physicists. They attend each other's meetings, present papers on associated problems, and utilize materials, techniques and instruments that, ten years

ago, they either had no interest in or had not heard of. Most importantly, they have come to speak a nearly common language, and thus to understand one another.

Such, then, is the force of a new and sweeping concept, which embraces all of biology, from viruses to whales, in a single unifying principle. With the discovery that nucleic acids are the chemical basis for heredity and that the biological phenomenon, identified as the gene, is in fact attributable to a specific polynucleotide sequence, molecular biology became a reality, and the long-hoped-for marriage between the biological and the physical sciences commenced.

Analysis of a Crystal

To exemplify this synthesis among scientific disciplines that have long had too little in common, I present here a single figure, which I have selected with some care (Fig. 1). A glance at this lovely gem, more valuable than a diamond, reveals that it a physical entity—a nearly perfect crystal with many sides. The magnification is low, and the crystal probably could be seen with the naked eye.

A crystallographer would undoubtedly assign a long name to this object, but despite the extraordinary power and resolution of his instruments, it is doubtful that he could precisely identify it.

A chemist would find that the crystal is composed of but two molecular species, one protein, the other nucleic acid, and could show that the nucleic acid is of the ribose type and makes up about 30 percent of the substance. But it is doubtful that he would establish the nature of the crystal.

A physical chemist would find that

the ribonucleic acid has a molecular weight of about 2 million, the protein a molecular weight of a few hundred thousand. He could also demonstrate that the crystal is entirely composed of like units with a particle weight of many millions, and he would infer that each particle contains both protein and nucleic acid. If he were very clever he could separate the two components that make up the particles, without destroying either, but he might need a biochemist to help.

An electron microscopist would find that the crystal is made up wholly of very tiny spheres, about 27 millimicrons in diameter, and he just might be able to discern that the central portion of each sphere had a slightly higher electron density than the peripheral area. He would not be able to visualize any limiting membrane, but, if he had had much experience with similar objects, he might begin to suspect the identity of the material. Certainly he would establish that the crystal contained several billion identical particles, for he could count them without great difficulty.

An immunologist would find that the crystal contains antigenic material and that it could stimulate the production of several kinds of antibodies in a number of different animal species. He would do well not to test it in this way in man or in monkeys, however, for if he did, and if he were a really competent immunologist, he could certainly identify the substance!

A virologist would make the startling discovery that the crystal is composed of type 1 poliomyelitis virus and that even a relatively small number of the particles, perhaps no more than 30, could induce severe paralysis in man or other primates. If, now, he obtained the ribonucleic acid that had been carefully separated from the protein component by the biochemist, he would find that it, too, is infective. Thus, he would have in his hands an *infective molecule* (how odd these two words seem when used together!)—one that can guide and direct the synthesis of more molecules like itself and ultimately lead to the production of disease.

A geneticist would find that the virus or the infective nucleic acid (the distinction has become merely semantic) possesses heritable properties which can be identified as genes, that it may undergo mutation as do other biological entities, and that the mutants have heritable properties which probably re-

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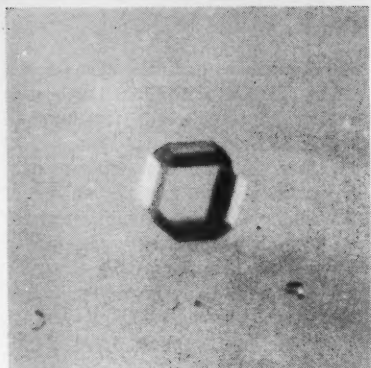


Fig. 1. A single large crystal of Mahoney poliomyelitis virus ($\times 80$). [R. L. Steere and F. L. Schaffer, *Biochim. et Biophys. Acta* 28, 241 (1958)]

flect alterations in the fine structure of their nucleic acids.

The lovely crystal has been found to have some surprising attributes. It is one of the first ever to be prepared with an animal virus, and I wish to acknowledge indebtedness to Wendell Stanley of the Virus Laboratory of the University of California for this excellent reproduction. To analyze in depth this seemingly simple object has required the kinds of professional competence that previously were distributed among some eight different scientific disciplines, both physical and biological. Because of the large significance to broad understanding that material of this kind contributes, biologists have recognized their need to acquire more than a nodding acquaintance with the physical sciences; at the same time, many in the latter disciplines have recognized the importance of knowing more biology. The results of this new community of interest—of the rebirth of the natural philosopher, if you will—have been both unexpected and remarkably rewarding.

Some Results

Not only are we confronted now with a number of infective molecules (some of the deoxyribonucleic acid type have recently been obtained from tumor-

inducing viruses), but also we can no longer escape a new biological concept—that of *infective heredity*. Certain bacterial viruses induce heritable changes in the bacteria they infect, as, too, of course, do several viruses that induce tumors in animals. A striking example is the diphtheria bacillus, which is led to produce a new protein—that is, diphtheria toxin—as a result of infection with a bacteriophage.

New genes now can be introduced into certain cells; genes previously present can be masked or overridden, and biological material is beginning to acquire a made-to-order aspect that recalls the remarkable achievements of synthetic organic chemistry. Heredity has acquired wholly new aspects, and the possibility that it may be controlled and guided seems no longer to be merely visionary.

Cytology and fine anatomical structure are being re-evaluated through systematic application of the electron microscope. Cytoplasm no longer appears to be simply a structureless jelly and has been revealed as a complex maze of channels and organelles with distinctive metabolic functions.

Chromosomes have been assigned individual designations, and aberrations in their number and variety are now associated with certain abnormalities in sexual development as well as with some congenital malformations—for example, mongolism. The mitotic apparatus has been separated from cells and studied as an independent entity. Why chromosomes cannot be visualized during the intermitotic interval remains a mystery.

The precise amino acid sequence of some proteins—for example, insulin and ribonuclease—is established, as is that of certain pituitary hormones. That the chemical structure of the latter substances had been exactly understood was proved when they were synthesized and shown to possess predicted biological activity. One type of human abnormal hemoglobin which is genetically determined is known to differ from the normal respiratory pigment only in respect to a single amino acid.

Immunology, possibly one of the

most important and also one of the most underdeveloped among the biological disciplines, is rapidly coming of age; recognition of the existence of so-called autoimmune mechanisms, the exquisiteness of the distinction between "self and non-self," to use Burnet's terms, and the remarkable advances in understanding homograft rejection are indicative of what lies ahead in this field. That immunology, like so much else in the life sciences, is shown to be directly under genetic control—control which is now known to be definable in molecular terms—is illustrative of the encouraging advancement and the progressive unification of scientific knowledge that is taking place.

Significance

I have emphasized the revolution that has occurred recently in biology in part because it is exciting but chiefly because of what it implies for understanding. The accumulation of seemingly unrelated technical details that has plagued and often discouraged the student of the life sciences is beginning to aggregate in a meaningful way, and much of it now hangs together in a framework of principles that are solidly based.

The discovery that a nucleic acid molecule can reproduce itself in a biological environment, that it carries in its chemical structure as much coded information as can be found in more than 100 textbooks, and that by virtue of chemical necessity it controls the synthesis of its complementary partner with such precision that mistake—that is, a mutation—occurs less than once in a million replications is not only impressive but far-reaching.

Biology, like chemistry, is in a position to discard many of its descriptive shackles. The unifying principles that emerged from knowledge of the structure of the atom, which so changed ideas in the physical sciences, now have their counterparts in new knowledge of the structure of the gene, which is, of course, the elementary basis for the continuity of life.

Science in the News

Disarmament: U.N. Agrees To Cancel Public Debate While U.S. and U.S.S.R. Talk Things Over

From New York. What had been feared would be a lengthy and acrimonious debate on disarmament at the United Nations took exactly 23 minutes last week, of which less than 5 minutes was taken by the principal adversaries. In a brief statement opening the "debate," Adlai Stevenson recommended that the topic be put off while the United States prepared its position for negotiations that, he hoped, would "produce results, rather than further disappointment." Andrei Gromyko, in an equally brief statement, announced that in view of the desire of the new Administration to complete its policy review the Soviet Union "found it possible not to insist" on a full debate until fall.

The two powers promised to carry on private discussions leading to full-scale formal negotiations this summer. The Canadian delegate said that the dropping of disarmament from the agenda until fall did not mean that the smaller powers were accepting the notion that disarmament is a private matter to be left to Russia and America, and he suggested that the two powers keep the U.N. informed of what they are up to in their private talks.

The meeting was more of a public performance than a public discussion. Except for some brief statements by African delegates echoing the Canadian position that disarmament and nuclear weapons are a matter of concern to the lesser as well as the great powers, the entire show was planned in advance, with everyone aware of what everyone else would say, including the fact that Krishna Menon, the Indian delegate, would say nothing. Several hours before the meeting began an American spokesman provided the

press with a briefing on what was going to happen, and the outcome, approval of a joint Soviet-American resolution putting off the debate until fall, was known before the meeting began.

The official American position is that the Russians, who originally wanted the debate, had quite unexplainedly agreed to put it off, and that they received no concessions. A minor Russian official, talking informally, suggested: "Gromyko talked to Kennedy alone, not even an interpreter present, so nobody knows just what happened; but we wanted to debate, now we agree not to debate; we must have gotten something."

A common view is that what the Russians got was American agreement to participate in bilateral negotiations with the Russians on disarmament, something which we have always refused in the past, if only on the grounds that our allies insisted on being included in the talks. The official American position is that this is not true: that the private Soviet-American discussions will deal only with setting up the formal basis for negotiations, not with questions of substance.

Hope for Progress

Whatever the details of the Soviet-American agreement, the effect of what happened last week was, first, to raise slightly hopes for real progress on disarmament, on the assumption that the Russian agreement to pass up the opportunity to insist on a battle of propaganda at the current U.N. session indicates that they are growing more serious about disarmament, and, second, to commit the U.S. more heavily than ever to coming up with specific proposals on disarmament in August, for we will surely look very silly at the next U.N. session in the fall if, after getting everyone to go along with our desire to take the better part of a year

to review our position, we come up with nothing new.

Just how much the Russian agreement to put off the disarmament debate indicated a real increase in the Russian willingness, or even ability, to deal realistically with the question is uncertain. There is somewhat less uncertainty about the sort of disarmament proposals the U.S. will make when its policy review is completed this summer.

The Soviet decision to put off debate was certainly influenced by the fact that the propaganda advantages to be gained, and therefore the temptation to insist on debate, had lessened with the change in the American administration.

What is sought is disarmament with inspection. The basic problem for the United States, and what made nearly everyone assume that it was the Russians who would get a propaganda advantage out of a U.N. debate today, is the necessity of the United States to worry, and consequently to talk, a great deal about the need for inspection, while the Russians feel free, and indeed are impelled, to talk a great deal about disarmament itself. The reasons for this, and for the greater appeal to other nations of the Russian approach, were reported in some detail here last fall (*Science*, 14 Oct.).

Russian Argument

The Russians last fall had no trouble finding sympathetic listeners, even among people sympathetic to the U.S., for their argument that the Americans were not really interested in disarmament, that we were only interested in "arms control," which, the Russians claimed, was just a device to open Russia to Western inspectors without doing anything much about disarmament. For themselves, the Russians insisted that they were perfectly ready to talk inspection if the Americans would only begin to talk specifically about disarming, and not just about control over existing arms.

The appeal of these arguments remains, but the fact that there is a new American government, and one which has, in general, favorably impressed the world, made it difficult for the Russians to make much of the propaganda advantage they might have in a debate. For there was a widespread willingness to accept the new Administration's contention that it needed time to prepare for serious negotiations, and consequently a willingness to listen to the

American argument, sure to be forthcoming if the Russians insisted on a full debate, that the Russians are more interested in stirring up controversy than in really trying to accomplish something on disarmament.

Thus the Russian agreement was not based solely on a willingness to give up making propaganda hay on disarmament, but partly at least on an awareness that there is not much hay to be made at the moment.

Soviet Attitudes

The American representatives at the latest Pugwash conference came away, in general, with the impression that the Russians were becoming more realistic in dealing with the problem of disarmament, but that they still had some way to go before really fruitful negotiations would be possible.

A favorable sign among the Russians has been a diminishment, not entirely satisfactory to the Americans, but noticeable, of the tendency of the Russians to dismiss American studies pointing up the pitfalls of various disarmament proposals as mere nitpicking thought up by people who are against disarmament anyway. Less favorable is the absence among the Russians of the sort of indisputably realistic talk about the arms race that one can find, at least on occasion, among Americans.

An interesting example of the way influential Americans can talk about the problems of disarmament was given in a telecast taped and distributed widely by WGBH, an educational station in Boston. Its panel was made up of members of the American delegation to the Pugwash (scientist-to-scientist) conference in Moscow last December, including Jerome Weisner, now special assistant to the President for Science and Technology, and W. W. Rostow, now deputy special assistant to the President for National Security Affairs.

Here is Weisner's comment on the Soviet concern that America might use arms inspection for espionage: "It (the concern) is real, and you can demonstrate this by an incident such as the U-2. In order to support our military strategy we have to have intelligence, and we pay a high price to get it. Therefore it is militarily important for them to keep us from getting it. Therefore it is not a price they are prepared to pay for trivial arms control or disarmament measures, and I think if I was negotiating for the Soviets or doing

their military planning, I would take this view too."

This is about as clear a presentation as a Russian could have given of the sort of factor that influences the Russians to take the position they do, and it is an important statement; for to recognize the other side's legitimate concerns is both a sign that you are taking the issue seriously and have thought it through carefully and an assurance that you will recognize a concession when it is made.

Unfortunately there is not much evidence yet that the Russians have brought themselves to see very clearly American interests as compelling as the Russian desire to protect their secrecy, and until they do so there is not much chance of agreement being reached on anything significant. The commonest Soviet attitude is to assume that the American negotiators may be sincere, but that they are held back by the evil forces of the Pentagon and the nasty capitalists.

Sputniks and Disarmament

There is also another disturbing factor, one that perhaps helps explain why the Russians have been slower than their American counterparts in really thinking through the problems of disarmament. This is that the Russians do not accept the existence of noncommunist nations. The serious American studies of disarmament have begun to grow into something important only in the past two or three years. They date, as do so many other recent developments, roughly from the Russian launching of the first sputnik.

This brought with it, of course, awareness that the age of intercontinental missiles is almost upon us, and a consequently more horrifying prospect of what a full-scale war would be like. But it also brought with it acceptance of the fact that Soviet power and technological achievement are strongly based and are roughly equivalent to our own, and consequently an abandonment of any real hope that the Soviet threat is just going to fade away, or even that it can be kept reasonably in hand by our maintaining the kind of overwhelming superiority in striking power we have enjoyed in the past.

Once you accept the fact that you are going to be in an arms race for a long time, and that you have no substantial prospects of being able to "win" this race, you begin to think more seriously of where it is leading

you not only in the foreseeable future of 2 or 3 years from now, but in the longer term future of 10 or 20 years; and although the view of this longer term future is cloudy, it is perceptible enough to be thoroughly disagreeable.

It is, again, easier to recognize the problems in the abstract than to really make them a part of your planning, for to do so requires you to make compromises on your more immediate objectives.

We seem to have become more and more realistic in our thinking about the arms race and disarmament as we have come to accept the idea that Soviet power is real, and that, if it is not permanent, it is certainly going to be around for a long time. Part of the difficulty in getting the Russians to be equally realistic is that they do not accept the idea that we are going to be around for a long time, at least not with power on a par with their own.

Prospects Cloudy

This suggests that one of the important factors that will affect disarmament prospects will be the success of our domestic and foreign policies in general. For our success will decide how much and how quickly we can alter the Soviet conviction that the tide of events in the world is going strongly in their direction, which tempts them with the idea that they only have to sit tight a few more years and we will no longer be such a real threat to them, or, at the least, that they will be able to get us to accept settlements on disarmament and other matters on their terms.

The net effect of this, ameliorated by some other factors, made more difficult by others, is that there is more optimism about the prospects for useful disarmament negotiations now than there has ever been before, when neither side was taking the subject very seriously except as a topic for propaganda warfare. But the outlook, nevertheless, can hardly be described as rosy.

A report on the likely product of the current American reappraisal of disarmament policy, based on the Administration's actions and statements, will appear here next week. In general, what can be expected above all is clarity; until now it has been almost impossible to find anyone who really claimed to know just what the American proposals meant and just what were the policy assumptions that underlay the proposals.—H.M.

News Notes

Cores Obtained from Beneath Deep Ocean Bottom for First Time

For the first time in history, man has taken cores from beneath the deep ocean bottom, according to an announcement by the National Academy of Sciences-National Research Council and the National Science Foundation. The cores were taken from under 11,700 feet of water near Guadalupe Island, off the western coast of Mexico.

Despite winds that averaged 25 miles per hour and 12-foot waves, the *CUSS I* drilling barge was held in position during the 61-hour drilling and coring operation.

The cores were obtained during experimental drilling for Project Mohole—a project set up to drill through the earth's crust to the mantle. Mohole is being carried out by the AMSOC Committee of NAS-NRC under grants from the National Science Foundation. The experimental drilling, under the direction of Willard Bascom, is being done by crews from Global Marine Exploration Company of Los Angeles, which owns and operates the *CUSS I*.

The diamond drilling bit first touched bottom at noon on 28 March. At 9 P.M. the first core, 53 centimeters long, was taken. The hole was then deepened to 234 feet below the ocean floor, and a second core, 60 centimeters long, was obtained. Both cores are firm, greenish-gray clay. They have been put aboard the *Spencer F. Baird*, oceanographic vessel of the Scripps Institution of Oceanography, University of California, for preliminary study.

The success of the experimental program demonstrates that scientists can now probe deep below the ocean floor to gain more knowledge about life as it existed many millions of years before man, and much more precise information about the age, composition, and structure of the earth.

U. S. and French Space Agencies Negotiate for Cooperative Research

In informal technical discussions in Washington, 20-21 March, representatives of the U.S. National Aeronautics and Space Administration and the French Comité des Recherches Spatiales affirmed their desire to cooperate in space science research of mutual in-

terest. A memorandum of understanding between the two agencies was released. It listed the following initial steps.

1) The Comité expects to make detailed proposals for experiments in the VLF, auroral and airglow, and biological fields, with the expectation that these experiments will be prepared by the Comité and flown, as mutually agreed, in appropriate scientific sounding rockets by NASA.

2) Further arrangements by the Comité are contemplated for the preparation of experiments to be incorporated in satellites to be launched by NASA, provided favorable results are obtained in rocket soundings.

3) The two organizations will exchange information regarding the design, equipment, and operation of a scientific sounding-rocket launching site. Such exchanges will include technical visits.

4) As an initial step toward mutual exchanges of personnel, NASA will accommodate, in its space science centers, technicians sponsored by the Comité.

What Is the Rate of Return on Investment in Education?

How much additional income does money spent on a college education yield? This fundamental question will be explored by the National Bureau of Economic Research with the aid of a \$75,000 grant from the Carnegie Corporation of New York. In the next 2 years the National Bureau will try to find out exactly how much all students, parents, alumni, corporations, foundations, governments (local, state, and federal), and others have spent on education—elementary, secondary, college, and on-the-job training—and how to calculate the rate of return on these investments in education.

From this and other information, Gary S. Becker, professor of economics at Columbia University and a member of the National Bureau's research staff, will attempt to determine what education contributes to a nation's economic growth. His conclusions are expected to be of particular value to new nations which face the problem of deciding whether to invest their limited funds in education or in industrialization.

In another phase, important to all nations, the study will investigate the

factors that influence college students in choosing a field of study and ways in which college courses govern their choice of occupation. Do students gravitate toward fields offering the highest earnings, the greatest opportunities for advancement, or the best opportunities for service?

News Briefs

Population of India. The population of India has been officially estimated at 438 million, according to a census completed in February. This represents an increase of about 21.5 percent in the last 10 years, a rise that is considerably above the most liberal of earlier estimates. By comparison, the population increase from 1941 to 1951 was 13.34 percent.

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Chartered plane to Europe. A group of AAAS members in the Boston area who are delegates to the International Pharmacology Congress in Stockholm and the International Chemotherapy Meeting in Naples, to be held next summer, plan to charter a plane for the round trip. The flight from Boston to Frankfurt will be on 17 August, and that from Paris to Boston, on 20 September.

There may be room on the plane for other conference delegates. Those interested in participating in the cooperative travel plan should communicate with Dr. Thomas C. Hall, Oncology Division, Medical Services, Lemuel Shattuck Hospital, 170 Morton St., Boston 30, Mass.

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Edison awards. At the Sixth National Mass Media Awards Dinner of the Thomas Alva Edison Foundation, held recently in New York, the following awards were among those presented.

Best science television program for youth. "Expedition!" accepted by Henry Plitt, president, American Broadcasting Company Films.

Special citation in recognition of brilliant leadership in the conception of the radio and television science series. "The Nature of Things" and "Science Review," to the Canadian Broadcasting Corporation; accepted by Keith Morrow, director of Radio and Television English Networks, Canadian Broadcasting Corporation.

Best children's science book. *Animal Clocks And Compasses*; accepted

by Margaret Hyde, author, and by Edward Booher, president, McGraw-Hill Book Company.

Best science book for youth. *Saturday Science*, by scientists of the Westinghouse Research Laboratories; accepted by Andrew Bluemle, editor, and Elliott B. MacRae, president, E. P. Dutton and Company.

Careers in science. A revised edition of *Careers in Science*, a selected bibliography for high school students, has been prepared by the AAAS Science Library Program. Compiled by program director Hilary J. Deason and William B. Blacklow, bibliographic assistant, the pamphlet lists 21 pages of publications helpful to high school students who plan to continue their education in a university or college, and more specifically, to those who are considering careers in the pure or applied sciences (including mathematics). The pamphlet, which costs 15 cents, may be obtained from the AAAS Science Library Program, 1515 Massachusetts Ave., NW, Washington 5, D.C.

International cooperation. Surgeon General Luther L. Terry has announced the first Public Health Service grants to U.S. universities to establish international centers for medical research in cooperation with foreign medical institutions. The grants were made to the University of California, Tulane University, Johns Hopkins University, and the University of Maryland. The awards are authorized by Public Law 86-610, which seeks to "advance international status of the health sciences through cooperative enterprises." Five million dollars was provided by Congress to launch the program.

Science in Antarctica. A comprehensive technical survey of geophysical, biological, and medical research in Antarctica has been prepared by the Committee on Polar Research of the National Academy of Sciences. In his foreword to the report, Laurence M. Gould, chairman of the committee and president of Carleton College, states that the purposes of the report are (i) to outline promising areas of scientific research in the Antarctic, (ii) to indicate the value and interest of antarctic studies to scientists throughout the nation, and (iii) to suggest the general importance of the United States antarctic research program as a national effort.

The work has been published in two

parts: part 1, *The Life Sciences in Antarctica*, and part 2, *The Physical Sciences in Antarctica*. A limited number of copies are available from the National Academy of Sciences, 2101 Constitution Ave., NW, Washington 25, D.C. (\$1.50 for each part).

Suicide rate. About 18,000 persons die by their own hand in the United States each year, according to the Metropolitan Life Insurance Company. This is at least twice the number of homicides and about 12 times the number of people killed in aircraft accidents of all kinds. Suicide ranks 11th among the causes of death; among white males, who account for about three-fourths of all suicides in the United States, it ranks eighth.

The relative frequency of suicide is appreciably higher in the United States than in Canada; the rates in 1958 were 10.7 and 7.5 per 100,000, respectively. The U.S. rate is several times that of Ireland, Greece, or a number of Latin American countries. On the other hand, our suicide rate is only half that recorded for Austria, Hungary, West Germany, or Japan.

Radioisotopes in industry. The Atomic Energy Commission has available for loan or for sale a new, 57-minute color motion picture, *Industrial Applications of Radioisotopes*. The 16-mm semitechnical film is a survey of the current uses of radioisotopes in American industry. It can be used for television projection, and is available from the commission's domestic and overseas film libraries.

Grants, Fellowships, and Awards

Crippling diseases. To make it possible for distinguished university professors to continue research activities after arbitrary retirement age, the Easter Seal Research Foundation of the National Society for Crippled Children and Adults, Inc., has announced creation of new awards to be known as Distinguished Service Awards for Professors Emeriti.

First recipient of one of the awards is the noted obstetrician Nicholson J. Eastman of Johns Hopkins University, who for 2 years will continue his study of the obstetrical background of cerebral palsy under an Easter Seal grant.

The new program is open only to retired full professors who devote substantial time to research and who will

have a continuing opportunity for research in a university or other major facility. Individuals in nonmedical fields related to rehabilitation of the crippled are also eligible for consideration. Further information may be obtained from the society's headquarters, 2023 W. Ogden Ave., Chicago 12, Ill.

North American fauna. The American Museum of Natural History has announced the establishment of the Theodore Roosevelt Memorial Fund to "help provide the necessary means of encouraging studies on the North American fauna to which Theodore Roosevelt, 26th President of the United States, devoted so much of his time and energy." Grants will be made to individuals conducting research in any phase of wildlife conservation or in related fields of North American natural history included in the activities of the American Museum.

Preferably, grants will be made to younger scientists, particularly to graduate students. Applications for grants for the current calendar year should be sent by 1 May to: Director, American Museum of Natural History, Central Park West at 79th St., New York 24, N.Y.

Scientists in the News

The Atomic Energy Commission has announced that five United States scientists have been selected to receive the Ernest Orlando Lawrence Memorial Award for 1961. The \$5000 awards will be presented on 28 April at AEC Headquarters in Germantown, Md., to the following men.

Leo Brewer, Lawrence Radiation Laboratory, University of California, Berkeley, for "singular contributions and leadership in the development of high temperature chemistry which have permitted major advances in reactor development."

Henry Hurwitz, Jr., General Electric Company Research Laboratory, Schenectady, N.Y., for "important contributions requiring unusual analytical skill and physical insight to the theory and design of nuclear reactors."

Conrad L. Longmire, Los Alamos Scientific Laboratory, Los Alamos, N.M., for "continued and original theoretical contributions, requiring unusual physical insight, to the development of nuclear weapons and the progress of plasma physics."

Wolfgang K. H. Panofsky, High Energy Physics Laboratory, Stanford

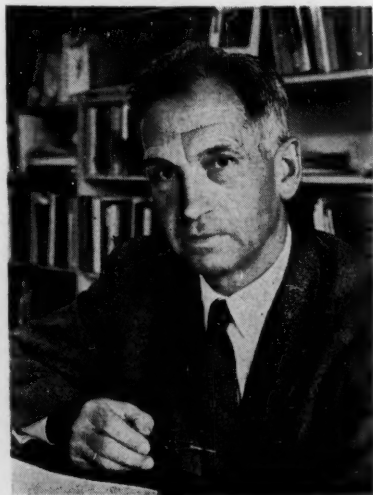
University, Palo Alto, Calif., for "outstanding contributions to nuclear physics and to the international control of nuclear testing."

Kenneth E. Wilzbach, Argonne National Laboratory, Argonne, Ill., for his "development of methods of tritium labelling of biologically important compounds which have permitted major advances in biology and medicine."

The commission is making the awards upon the recommendation of its General Advisory Committee and with the approval of the President. Assisting the Committee in the preliminary screenings of the nominations were the AEC Advisory Committee for Biology and Medicine and four panels of distinguished scientists and engineers in the fields of physics, chemistry and metallurgy, weapons, and reactors.

Ernst Mayr, Alexander Agassiz professor at Harvard University's Museum of Comparative Zoology, will succeed Alfred S. Romer as director of the museum on 1 July. Romer, who leaves the directorship after 15 years in the post, will continue to teach and to do research at Harvard.

George Cunningham, Sir William Collins professor of pathology at the Royal College of Surgeons, London, is spending the month of April as visiting professor of pathology at the State University of New York Downstate Medical Center in Brooklyn. He is particularly interested in the problem of lung cancer and is expected to lecture on this subject during his stay at the Medical Center.



Ernst Mayr

Luther L. Terry has been sworn in for a 4-year term as Surgeon General of the U.S. Public Health Service. Terry, whose appointment by President Kennedy was confirmed by the Senate last month, succeeds **Leroy E. Burney**, who resigned on 30 January.

The Silliman Memorial Lectures for 1961 at Yale University will be given by **René J. Dubos** of the Rockefeller Institute. The series, entitled "Medical Future of Human Populations," will be given at 5 P.M. on four successive days, 17-20 April.

The American Heart Association has named **Earl H. Wood** of Rochester, Minn., to the lifetime post of career investigator. Wood is professor of physiology at the Mayo Foundation, University of Minnesota Graduate School, and consultant in physiology to the Mayo Clinic. His appointment is the tenth in the career investigatorship category, which was established by the Heart Association 10 years ago.

Jesse L. Greenstein, of the California Institute of Technology, will discuss "Stellar Evolution and the Origin of the Chemical Elements" as a Sigma Xi national lecturer at a number of colleges during April and May.

The American Society of Zoologists has announced that the following corresponding members have been elected by the executive committee: **B. L. Asataurow**, Moscow, U.S.S.R.; **F. Baltzer**, Bern, Switzerland; **Louis Gallien**, Paris, France; **Giuseppe Montalenti**, Naples, Italy; **C. F. A. Pantin**, Cambridge, England; **B. Rensch**, Münster, Germany; **Paulo Sawaya**, São Paulo, Brazil; **Gunnar Thorson**, Helsingör, Denmark; **Nikolaas Tindergen**, Oxford, England; and **Tohru Uchida**, Sapporo, Japan.

Cecil W. Mann, professor of psychology at Tulane University, will retire on 31 May. As of 1 September, he will be professor of psychology at Western Carolina College at Cullowhee, N.C., where he also expects to teach in the summer session.

J. Rubin, chairman of the department of soils and water, Israel National and University Institute of Agriculture, Rehovot, and associate professor at Israel Institute of Technology, is now on leave in the United States. He will be at the University of California, Berkeley, until June.

Recent Deaths

Harry L. Fisher, Claremont, Calif.; 76; an authority on rubber chemistry and technology, who for 4 years before his retirement in 1957 directed research at the Rubber Technology Foundation of the University of Southern California; in 1954, was president of the American Chemical Society; held 56 patents; taught at Columbia University, from 1912 to 1919; was a research chemist for the Goodrich Rubber Company for 7 years, and for the U.S. Rubber Company for 10 years; 9 Mar.

Norman Gilbert, Winter Park, Fla.; 86; emeritus professor of physics at Dartmouth College, where he taught for 42 years, beginning in 1903; visiting professor of physics at Rollins College until 1952; wrote two popular textbooks on physics; 21 Mar.

John F. Hennion, Piermont, N.Y.; Columbia University specialist in marine seismic refraction and reflection; was chief research scientist aboard the university's research ship *Vema*, now on an expedition off the west coast of South America; 17 Mar.

Isfred I. Hofbauer, Cincinnati, Ohio; 89; a leader in modern gynecology and obstetrics, who was one of the first to use hormones to avoid some dangers of childbirth (the Hofbauer cells in the placenta are named for him); conducted extensive research in endocrinology; was associate professor of obstetrics at Johns Hopkins University before accepting appointment, in 1933, as associate professor of obstetrics at the University of Cincinnati; 13 Mar.

Henry N. Kenwell, Buffalo, N.Y.; 60; chief surgeon at Millard Fillmore Hospital, Buffalo, and associate professor of surgery at the University of Buffalo Medical School; 13 Mar.

Esper S. Larsen, Jr., Washington, D.C.; 81; for 25 years taught mineralogy and petrography at Harvard University, retiring as professor in 1949; geologist with the U.S. Geological Survey from 1918 to 1923 and (upon his retirement from Harvard) from 1949 to 1958; a member of the National Academy of Sciences and recipient of many honors in geology; 7 Mar.

Max Mason, Claremont, Calif.; 83; mathematical physicist and a former president of the University of Chicago and of the Rockefeller Foundation; had taught at Massachusetts Institute of Technology, Yale University, the University of Wisconsin, California Institute of Technology, and Claremont Men's College; 23 Mar.

Book Reviews

Television in the Lives of Our Children.

Wilbur Schramm, Jack Lyle, and Edwin B. Parker. Stanford University Press, Stanford, Calif., 1961. vii + 324 pp. Illus. \$6.

The Impact of Educational Television.

Wilbur Schramm, Ed. University of Illinois Press, Urbana, 1960. 247 pp. \$5.

Television in the Lives of Our Children is the first comprehensive research report on the social and psychological impact of commercial television on American children. It closely parallels in research design and conclusions the British study prepared by Himmelweit, Oppenheim, and Vince, *Television and the Child*.

The senior author, Wilbur Schramm, is a professor of communications research at Stanford University, a professional writer with a great variety of experience, and a person committed to the concept of self-regulation of the mass media by the present owners and managers. He is not only interested in analyzing the consequences of the mass media, but also in pointing the direction for social policy. Because he is sympathetic to the present organization of the mass media and is not a rabid critic of "mass culture," his findings and recommendations stand as the most sober and critical evaluation of television yet produced. Despite his balanced language, Schramm implicitly and explicitly calls for major modifications in television programming for children.

The basic design of the research involved the administration of questionnaires and interviews to a variety of samples of children, including some drawn from two Canadian towns, one of which had not been exposed to television. The frame of reference is broader than the stimulus-response model that dominates much communications research, in that the authors are fully aware of the audience's active role in selecting and using television for its needs. Unfortunately, the authors do

not investigate how the decisions on programming are made, or why the directors of television conclude that only a diet of overwhelming violence and crime is appropriate for American children.

Schramm and his associates describe, with scientific precision, this overwhelming concern with crime and violence in the programs produced for children. They document the oceanic quality of television in the daily lives of children, nine out of ten of whom expose themselves to the medium by the time they reach the first grade. By the time they reach the sixth or seventh grade, children spend three to four hours a day watching TV; this begins to fall off slowly throughout high school. Television dominates the leisure time activities of its audiences. It cuts into movie attendance, radio listening, and reading. It reduces time for play.

Children's Reactions

Television has high prestige among children. Exposure to commercial television seems initially to increase the vocabularies of the brightest and the slowest children; however, these advantages decline as the child progresses through school. The bright child who was a heavy user of television will score less well on knowledge tests and will do less well in school than a light user. In their teens, the bright children considered television less important and less necessary to prestige than children who were not so bright. In short, intelligence and motivation can and do conquer the TV medium. In fact, as the child grows older, he uses printed media for reality experiences and serious learning.

The authors try hard to affirm that television broadens horizons, but in the end the best that they can say is "we do not say that television does not or can not stimulate a child to broader horizons; merely that it seems not to do those things in any greater degree than takes place in the absence of tele-

vision." It may increase their knowledge of popular singers but not especially their knowledge of topics closely related to public affairs or their knowledge of subjects chiefly learned in school—for example, science.

The authors make much of what they see as a sharp difference between "fantasy" and "reality" experiences developed by exposure to television. But fantasy and reality reactions are more interwoven than they assume. The development of a sense of reality depends on certain types of fantasy experiences which are difficult to identify. Nevertheless, their findings in this area are worth while, for they confirm other studies showing that children who have unsatisfactory relations with their family or peer groups tend to retreat into television. It is refreshing, however, that Schramm and his associates do not therefore claim that television is a passive agent in this process but rather go on to demonstrate how television in turn contributes to the reinforcement of undesirable fantasy and heightened antisocial aggression. This relationship between unsatisfactory social relations, exposure to mass media, and, in turn, increased aggression, is sharper among middle-class than among lower-class children. Children are mainly frightened when harm involves cutting, stepping in a trap, or some nonritual violence. They are frightened, particularly, when they view such programs in dark rooms or alone.

Exposure to commercial television is not seen as an advantage or as a barrier to success in school. Nevertheless, it does in some cases contribute to passivity in children, although long-term studies will be required to determine the lasting effect. "But the best way to avoid excessive passivity in our children is not to give them television as a mother-substitute in early life; rather to make them feel loved and wanted at home and, so far as possible, to surround them with friends and activities." The authors answer the complex question of the link between television's emphasis on violence and delinquency with "television is at best a contributory cause." But as a contributory cause, they do not deny its relevance.

Educational Television

The Impact of Educational Television is a collection of research studies dealing with educational television broadcasting. The effort was sponsored by the National Education, Television and Radio Center, which made 50 research

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grants-in-aid for educational research during the period 1956-59. In a chapter entitled "A decade of teaching by television," Hideya Kumata summarizes the available data on the use of TV in classroom situations. The basic finding, derived from almost 300 comparisons, is that there is no significant difference, in the overwhelming number of observations, in the amount of immediate information gained when students taught by television are compared with students taught under face-to-face conditions. Moreover, the same result holds true for the retention of subject matter. Superiority of television is reported more often in voluntary audience situations than in captive audience situations. Thus the differences are in motivations among audiences rather than in the fact of transmission.

Superiority of television is reported more often in the lower than in the higher educational levels, presumably because of the greater suggestibility of children. Attitudes toward television and toward the subject matter are of prime importance, for students learn less when they have a negative attitude toward TV, and the negative attitude increases with age and educational level. Moreover, measuring the intangibles of education—those aspects beyond mere assimilation of information—has not been adequately studied. Thus, there is now at hand an impressive body of data indicating that classroom television is no magical resource.

When radio was first developed, there were great hopes for its potential as an educational device. Radio never achieved a level commensurate with these hopes, but after a long rather dormant period, university radio has found an active role in the educational division of labor. The initial aspirations for television were even greater, and pressure for the success of television far exceeds that involved in the history of radio. The Ford Foundation has become a major pump primer in television; in universities and to a much greater extent in high schools and public school systems, extensive resources are being allocated. There is every reason to believe that television will have greater success as an educational medium than radio. In the decade ahead, given the tremendous expansion of public school enrollment and the great pressure on schools to expand their custodial and recreational functions, television will become an indispensable resource. But these research observations clearly indicate that television will find its role

in the educational system not because of its over-all pedagogical superiority but because of the great pressures for economic savings which face the school system. When TV is used as a resource—as chalk, the blackboard, maps, and the field trip are used—it can apparently serve to augment teaching facilities. But the great danger lies in the possibility that the United States will develop a two-track system, in one segment of which television is used heavily as a mass recreational device.

Much less is known about the impact of educational television from the special stations that transmit to the general public. In the suggestive essay by Ken Geiger and Robert Sokol, "Educational television in Boston," it appears that there are two rather distinct audiences for educational broadcasts. One is a small group of college-trained and college-oriented people who consume educational programs as they would any other form of adult education. For a larger group of much lower educational background and, by implication, of blocked social mobility, the educational programs are transformed into a kind of entertainment or popular culture. Thus, the informal network of educational television stations broadcasting to the public at large may become, in effect, a competitor of the national commercial systems and offer a form of popular culture more compatible with fundamental American values than that currently presented by commercial stations.

Social and Psychological Consequences

While Schramm's research does not conclude that television is ruining or debasing our society, it is now impossible for the managers of commercial television to deny the social and psychological consequences of their medium. The further growth of educational television will be only a partial solution to the questions concerning "television and our children" raised by this study. Commercial television, because it fills so great a part in the lives of youngsters, will have to find its own formula. Competition between networks can hardly supply the basis, for such competition, in the struggle to reach the largest audience, more often debases content. Instead, self-regulation, standards set by the Federal Communications Commission, and active involvement by educational, parental, and civic associations become the instruments of social change. One has only to observe the experiments of the Canadian Broad-

casting Corporation: limited funds and less pressure have produced a simpler but more satisfactory programming policy for children.

Schramm's research is also relevant for the development of educational television. If national policy continues to stimulate the growth of educational television stations, the result will be an important alternative to commercial television for the general public. Already there is evidence that commercial television is increasing its output of documentary and public service programs. Thus, competition of this kind will increase standards, if the educational stations are guaranteed an economic base of operation independent of the size of their audience. But the future of educational television depends on classroom use. The research completed to date is only the first step, in that exaggerated claims have been cut down to size. The next step is to study the consequences of educational television on the school systems, not merely on the individual student. What is the impact of television on the teacher? What new skills and techniques are required to integrate this teaching device into the school system? Does the faculty lose control of curriculum when elaborate television productions are introduced? Such questions become crucial if the potentialities of classroom television are to be realized without destroying the autonomy of the teacher.

MORRIS JANOWITZ

Department of Sociology,
University of Michigan

Plant Physiology. A treatise. vol. 1A, *Cellular Organization and Respiration*. vol. 1B, *Photosynthesis and Chemosynthesis*. F. C. Steward, Ed. Academic Press, New York, 1960. vol. 1A, xxvii + 331 pp., illus., \$13; vol. 1B, xvii + 348 pp., illus., \$12.

These volumes follow volume 2 in an intended series of six volumes. Volume 1A has three articles treating cellular organization and respiration; volume 1B treats photosynthesis and chemosynthesis in single articles. Two of the five articles deal chiefly with higher plants: these are "The Plant cell and its inclusions" by R. Brown (in vol. 1A) and "Energy storage: photosynthesis" by Hans Gaffron (in vol. 1B). The first of these is a reasonable treatment in the 126 pages allowed, but it is poorly illustrated for a subject chiefly

concerned with the appearances of structures. The Gaffron article on photosynthesis (272 pages) is thoughtful and very thorough; it well summarizes the rapidly advancing subject as of 1958. An advantage of a limited treatise on photosynthesis is that the myriad of early and less pertinent observations cannot be included.

The other three articles — namely, "Proteins, enzymes, and the mechanism of enzyme action" (74 pages) by Birgit Vennesland (in vol. 1A); "Cellular respiration" (105 pages) by D. R. Goddard and W. D. Bonner (in vol. 1A) and "Chemosynthesis: the energy relations of chemoautotrophic organisms" (40 pages) by M. Gibbs and J. A. Schiff (in vol. 1B)—are needed in a general treatise on plant physiology. Their essential content is drawn from the wider aspects of biochemistry and is very condensed. The article by Birgit Vennesland is interesting to read and is a reasonable integration of the action of enzymes in groups rather than separately. In a preamble the editor comments that understanding energy storage requires consideration of chemosynthesis as well as photosynthesis, which accounts for the article on chemosynthesis. Oxidation and reduction and electron transport through cytochrome systems are particularly well treated by Goddard and Bonner. Their discussion of pathways of fermentation suffers from terseness, as is so apt to be the case for this subject.

A general treatise might be assessed on the basis of its organization of the content of the subject, the selection of authors and their thoroughness and enthusiasm, the inclusion of the most recent material as well as classical aspects, and on being sufficiently vital to arouse interest. This series fully meets these criteria.

S. B. HENDRICKS

Mineral Nutrition Laboratory,
U.S. Agricultural Research Service

Biology and Comparative Physiology of Birds. vol. 1. Alexander J. Marshall, Ed. Academic Press, New York, 1960. 518 pp. Illus. \$14.

Birds have been used as research material by so many biologists and in so many kinds of investigations that the resulting literature has become voluminous and scattered to such a degree that it is a major task for any investi-

gator to acquaint himself with the available data. Any attempt to bring together a critical, coordinated, modern synthesis of large segments of these fields of study is therefore apt to be welcomed by the harassed zoologist. Indeed, Marshall first decided to undertake the preparation of this work because he himself was acutely aware of the time and trouble involved in gathering the information needed for his own researches. Once embarked upon this comprehensive survey, he found it necessary to enlist the help of some 23 highly competent colleagues in England, on the continent, and in the United States, Canada, and Australia. Of the 23, 13 have contributed chapters to this first volume (volume 2 is scheduled for publication shortly): "The origin of birds" by W. E. Swinton; "Adaptive radiation in birds" and "Classification" by R. W. Storer; "Geographical distribution" by D. L. Servery; "Development" by R. Bellairs; "The integumentary system" by M. E. Rawles; "Skeleton" by A. d'A. Bellairs and C. R. Jenkin; "Musculature" by A. J. Berger; "Blood-vascular system" by J. R. Simons; "Respiratory system" by G. W. Salt and E. Zeuthen; "Digestive system" by D. S. Farner; and "Excretion" by I. Sperber.

Each chapter begins with a carefully worded introduction, which quickly and easily orients the reader to the viewpoints and guiding thoughts underlying the presentation. After this comes a series of subheads (the number varies in the different chapters from a minimum of 3 to a maximum of 18) and finally a useful and well-selected list of literature references. It is somewhat invidious to single out special chapters for mention, but just as an example of the convenient subdivisions in which the factual matter is presented and discussed, we may take the following two. In the chapter devoted to adaptive radiation, the breakdown is as follows: introduction; problems in size, the surface-volume ratio; locomotor adaptations; feeding adaptations; adaptive radiation within families of birds; the history of adaptive radiation; references. The chapter on respiration includes: introduction; anatomy; ventilation of the respiratory tract while standing; the regulation of respiratory movements; heat regulation by the respiratory system; respiration during specialized activities; references.

The chapters vary in the amount of detailed information presented, but all

seem to be not only adequate but decidedly useful and reliable digests and guides.

The book is designed not only for ornithologists but also for general biologists who may want information about a given topic in avian biology. It can be recommended heartily to both groups as a reference work and for browsing. Two indexes, subject and author, complete this notable volume and make readily available the vast number of topics surveyed in it.

HERBERT FRIEDMANN

U.S. National Museum,
Smithsonian Institution

British Cup Fungi and Their Allies. An introduction to the Ascomycetes. R. W. G. Dennis. Published for the Ray Society by Quaritch, London, 1960. xxiv + 280 pp. Illus. + plates. 80s.

The author has brought together, in excellent fashion, an account of the Ascomycetes of England, of which the cup fungi form an important part. The book is issued as Number 143 of the Ray Society series (a series of impressive scientific books in many fields published since 1844. A similar work on the Ascomycetes of North America has never been published.

An introductory chapter covers effectively such topics as fungi in general, structure and classification of the Ascomycetes, taxonomy and nomenclature, and techniques recommended for those who wish to collect and study these interesting organisms. The body of the text presents concise, accurate descriptions of each order, family, and genus involved, with effective keys for their ready separation. Species are not keyed, but they are carefully, though briefly, described with emphasis necessarily on microscopic characters.

The outstanding feature of the book is to be found in the illustrations, which are from the collections of the Royal Botanic Gardens at Kew. Nearly 500 species are depicted in the 40 colored plates and more than 150 others in black-and-white plates. Even though it is restricted geographically, this book will be very useful to all who are concerned with the Ascomycetes, for a great many of the species included are of world-wide distribution.

JOHN A. STEVENSON

4113 Emery Place, NW,
Washington, D.C.

Stationary Processes and Prediction Theory. Harry Furstenberg. Princeton University Press, Princeton, N.J., 1960. x + 283 pp. \$5.

There are several books which discuss the topic of this title and give salient analytical results dealing mainly with linear prediction. In this volume Furstenberg treats the concept of predictability—that is, what sequences are predictable in a specified sense—without limiting himself to the linearity assumption. Because of the general nature of the discussion, the results are mainly theoretical, and practical computational methods are mentioned only in passing. This book is strictly for the pure mathematician, and it will be difficult reading for all but a very few.

GEORGE WEISS

University of Maryland

Polythene. The technology and uses of ethylene polymers. A. Renfrew and Phillip Morgan, Eds. Iliffe, London; Interscience, New York, ed. 2, 1960. xxi + 781 pp. Plates. \$25.75.

Man's scientific and technical knowledge of ethylene polymers and copolymers is presented here in a well-organized and well-written manner. The topics considered range from the theory and kinetics of ethylene polymerization through the chemical engineering aspects of manufacture, structure, properties, testing, specifications, processing techniques, and formulation to areas of specific application. The full gamut of ethylene polymers with respect to molecular weight, melt index, and density is treated. It is a monumental and extremely valuable treatise. The editors have done a particularly commendable job in maintaining a high degree of uniformity in style and readability.

Some topics are not treated in detail or as thoroughly as might be expected from the general quality of the book. For instance, the treatments of the tear, puncture, impact, and clarity properties of film and sheeting and of the bursting strength and working stresses of pipe are relatively incomplete and thus are apt to be misleading. The material on processing equipment is mainly concerned with British machinery, although the text is in general written around the principles concerned; thus American, German, Italian, and other foreign counterparts can be identified by ex-

perts in this phase of plastics engineering.

The editors emphasized the basic scientific aspects of ethylene polymers; this is fully justified because the technological aspects are based on the principles. It is this area that is given the most thorough treatment. The plastics engineering aspects embodied in the chapters on processing techniques are second in thoroughness of treatment, although a few of the topics are not developed as thoroughly as they might be. The majority of the topics covering applications could be treated more extensively, but in most cases, this would not be warranted. In general, the editors have arrived at a reasonable balance in the amount of space devoted to the four areas: basic science, chemical engineering, plastics engineering, and technology.

I did not note any factual errors. However, some chapters in the sections on techniques and applications do not have literature references. It is difficult to feel confident that a topic has been considered adequately when no literature citations are provided. To the scholarly reader this must be exasperating.

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New Books

Mathematics, Physical Sciences, and Engineering

Adaptive Control Processes: A Guided Tour. Richard Bellman. Princeton Univ. Press, Princeton, N.J., 1961. 271 pp. \$6.50.

Advances in Polarography. vols. 1-3. Ian S. Longmuir, Ed. Pergamon, New York, 1960. 1235 pp. Illus. \$45. Proceedings of the second international congress, 1959.

Aerosols: Science and Technology. H. R. Shepherd, Ed. Interscience, New York, 1961. 562 pp. Illus. \$22.50.

Applied Statistical Decision Theory. Howard Raiffa and Robert Schlaifer. Graduate School of Business Administration, Harvard Univ., Boston, Mass., 1961. 374 pp. \$9.50.

Applied Thermodynamics. Stanley H. Bransom. Van Nostrand, Princeton, N.J., 1961. 237 pp. Illus. \$6.

Avionics Research: Satellites and Problems of Long Range Detection and Tracking. E. V. D. Glazier, E. Reichtin, and J. Voge, Eds. Pergamon, New York, 1960. 267 pp. Papers presented at the AGARD Avionics Panel Meeting, held at Copenhagen in October 1958.

Boolean Algebra and Its Applications. J. Eldon Whitesitt. Addison-Wesley, Reading, Mass., 1961. 192 pp. Illus. \$6.75.

The Chemistry of the Terpenes. A. R. Pinder. Wiley, New York, 1960. 230 pp. \$8.25.

Complex Variables and the Laplace Transform for Engineers. Wilbur R. LePage. McGraw-Hill, New York, 1961. 492 pp. Illus. \$12.50.

The Continuous Casting of Steel in Commercial Use. K. P. Korotkov, H. P. Mayorov, A. A. Skvortsov, and A. D. Akimenko. Translated from the Russian by V. Alford. H. T. Protheroe, Ed. Pergamon, New York, 1960. 181 pp. Illus. \$8.50.

Cumulus Dynamics. Charles E. Anderson, Ed. Pergamon, New York, 1960. 220 pp. \$12. Proceedings of the first conference on cumulus convection, held in May 1959.

Dictionary of Mechanical Engineering. Alfred Del Vecchio. Philosophical Library, New York, 1961. 354 pp. \$6.

Electronics in Engineering. W. Ryland Hill. McGraw-Hill, New York, ed. 2, 1961. 350 pp. Illus. \$8.

Elements of Physics. For students of science and engineering. George Shortley and Dudley Williams. Prentice-Hall, Englewood Cliffs, N.J., ed. 3, 1961. 957 pp. Illus. Trade, \$13.35; text, \$10.

An Engineering Approach to Gyroscopic Instruments. Elliott J. Siff and Claude L. Emmrich. Robert Speller and Sons, New York, 1960. 134 pp. \$7.50.

Essentials of Dielectromagnetic Engineering. An introduction to the thinking in and the use of ferrites and high-permittivity dielectrics. H. M. Schlicke. Wiley, New York, 1961. 264 pp. Illus. \$9.50.

Field Emission and Field Ionization. Robert Gomer. Harvard Univ. Press, Cambridge, Mass., 1961. 195 pp. Illus. \$6.75.

Homology Theory. An introduction to algebraic topology. P. J. Hilton and S. Wylie. Cambridge Univ. Press, New York, 1960. 499 pp. Illus. \$14.50.

General College Chemistry. Charles William Keenan and Jesse Hermon Wood. Harper, New York, ed. 2, 1961. 758 pp. Illus. \$3.25.

Die Geologie Mittelamerikas. Richard Weyl. Borntraeger, Berlin, 1961. 241 pp.

Hyperstatic Structures. An introduction to the theory of statically indeterminate structures. vol. 2. J. A. L. Matheson and A. J. Francis. Academic Press, New York; Butterworths, London, 1960. 293 pp. Illus. \$11.

Large Elastic Deformations. And non-linear continuum mechanics. A. E. Green and J. E. Adkins. Oxford Univ. Press, New York, 1961. 361 pp. \$8.80.

Linear Systems Analysis. An introduction to the analysis of discrete-parameter time-invariant linear systems. Paul E. Pfeiffer. McGraw-Hill, New York, 1961. 555 pp. \$12.50.

Modern Chemical Processes. vol. 6. By the editors of *Industrial and Engineering Chemistry*. Reinhold, New York, 1961. 120 pp. Illus. \$6. Seventeen articles reprinted from 1958 and 1959 issues of the journal.

Modern Fundamentals of Algebra and Trigonometry. Henry Sharp, Jr. Prentice-Hall, Englewood Cliffs, N.J., 1961. 349 pp. Trade, \$8.65; text, \$6.50.

Reports

Oxygen Consumption of Tissues in the Human Lung

Abstract. A method for estimating the metabolic rate of the human pulmonary tissues is described. Six patients with far advanced pulmonary tuberculosis showed an average rate of 12 percent of the total oxygen consumption. A method for measuring the right ventricular output with an inert gas is also outlined, and the use of this approach to minimize errors in the estimation of the tissue metabolic rate is described.

Little is known about the metabolism of human pulmonary tissues. The only study cited in the recently published "Handbook of respiration" is that of Krebs (1) who found that lung tissue from a human embryo consumed 3.7 mm³ of oxygen per hour per milligram of dry weight. While this figure can be used to calculate the oxygen consumption of the lungs within the body, the accuracy of the calculation is uncertain. No alternative is available, however, since direct measurements have not, to our knowledge, been made in living man.

The pulmonary tissues have access to several sources of oxygen, including the air in the alveoli, the blood in the pulmonary vessels, and the blood draining from the bronchial circulation into the pulmonary veins and arteries. Whether the tissues utilize all of these sources is uncertain. The consensus is that the alveolar walls derive oxygen chiefly from the alveolar air, while the bronchi, the smaller air passages, and major portions of the visceral pleura utilize oxygen carried by the bronchial flow. A fourth source, the bronchial-

hemiazzygos blood-flow, supplies oxygen to the main stem bronchi and their first two subdivisions. The oxygen consumed by these structures, which lie partially within the mediastinum, is not included in the analysis that is presented below.

Figure 1 depicts the exchanges of oxygen which theoretically can take place within the lungs. Inspection of the drawing provides a basis for summing the rates at which oxygen enters and leaves the intravascular volume delineated by vertical hatching.

$$\dot{Q}_R C_{\bar{v}O_2} + \dot{Q}_B C_{B_{O_2}} + \dot{V}_{O_2} - \dot{V}_{T_A} - \dot{V}_{T_C} - (\dot{Q}_R + \dot{Q}_B) C_{a_{O_2}} = 0 \quad (1)$$

where \dot{Q}_R = volumetric flow from the right ventricle; \dot{Q}_B = volumetric flow from the bronchial arteries draining into the pulmonary vessels; $C_{a_{O_2}}$ = concentration of oxygen in the arterial blood; $C_{\bar{v}O_2}$ = concentration of oxygen in the mixed venous blood; $C_{B_{O_2}}$ = concentration of oxygen in the bronchial blood draining into the pulmonary vessels; \dot{V}_{O_2} = oxygen uptake measured at the mouth; \dot{V}_{T_A} = oxygen supplied to the pulmonary tissues by the alveolar air; and \dot{V}_{T_C} = oxygen supplied to the pulmonary tissues by the pulmonary blood flow.

It should be emphasized that \dot{V}_{T_A} and \dot{V}_{T_C} represent potential, not proven, exchanges of oxygen. They are included in the equation for the sake of generality.

In a similar way, an equation can be written to describe the oxygen exchange in the intravascular volume defined by oblique hatching. Thus

$$\dot{Q}_B C_{a_{O_2}} = \dot{V}_{T_B} + \dot{Q}_B C_{B_{O_2}} \quad (2)$$

where \dot{V}_{T_B} = oxygen supplied to the pulmonary tissues by the bronchial blood flow.

Adding Eqs. 1 and 2 yields the following expression:

$$\dot{V}_{T_A} + \dot{V}_{T_B} + \dot{V}_{T_C} = \dot{V}_{O_2} - \dot{Q}_R (C_{a_{O_2}} - C_{\bar{v}O_2})$$

The three terms of the left-hand member represent the oxygen extracted, respectively, from the alveolar air, the bronchial flow, and the pulmonary flow.

Hence, the sum of these terms ($\dot{V}_{T_A} + \dot{V}_{T_B} + \dot{V}_{T_C}$) is an estimate of the metabolic rate of the pulmonary tissues.

$$\dot{V}_{T_{O_2}} = \dot{V}_{O_2} - \dot{Q}_R (C_{a_{O_2}} - C_{\bar{v}O_2}) \quad (3)$$

The equation indicates that the calculation of $\dot{V}_{T_{O_2}}$ entails measuring the flow from the right ventricle (\dot{Q}_R), the oxygen uptake at the mouth (\dot{V}_{O_2}), and the concentrations of oxygen in the arterial ($C_{a_{O_2}}$) and mixed venous ($C_{\bar{v}O_2}$) blood. \dot{Q}_R can be measured from a dye-dilution curve inscribed through a cardiac catheter with its tip in the pulmonary artery (2), \dot{V}_{O_2} can be obtained by using a Scholander microanalyzer, and $C_{a_{O_2}}$ and $C_{\bar{v}O_2}$ can be determined by Van Slyke's method.

In an earlier study we compared the outputs measured by the Fick and dye-dilution methods in patients with either heart disease, bronchiectasis, or minimal tuberculous infections (3). Our results, like those of others, showed that the two measurements agreed well in the majority of patients, and that the difference between the two had a random distribution. These observations suggested that the oxygen consumed by the pulmonary tissues lay within the errors of the measuring techniques. But a series of patients with advanced pulmonary tuberculosis presented a unique pattern in that the Fick output almost always exceeded the dye output by a small amount. One possible explanation was that the presence of tuberculosis interfered with the methods of measurement, causing either an underestimation of flow by the dye principle or an overestimation of flow by the conventional Fick. However, there was no reason to believe that the results could be attributed to such artifacts of measurement. Thus, we favored the alternative explanation that a small part of the oxygen accounted for in the Fick calculation was, in reality, metabolized by the lungs.

This reasoning led to the present study in which the metabolic rate of the pulmonary tissues was calculated

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should not repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to one 2-column figure (that is, a figure whose width equals two columns of text) or to one 2-column table or to two 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [Science 125, 16 (1957)].

in six patients with severe pulmonary tuberculosis. Three estimates were obtained in four of the patients and two estimates in two. Of these 16 values two were negative. The remaining 14 indicated that the pulmonary tissues consumed an average of 12 percent of the total oxygen consumption of the body. The range extended from 0 to 20 percent.

While the average rate of 12 percent seems a high figure, two lines of evidence provide support for its validity. The first is that inflammation enhances metabolic activity, and the second is that patients with advanced tuberculosis sometimes display a high metabolic rate. On the basis of these observations, it seems reasonable to think that part of the extra oxygen consumed by such patients is metabolized by the inflamed tissues in the chest. That the metabolic rate of normal lungs is lower can be inferred from experiments performed in animals. Dawes and his colleagues (4) calculated the oxygen consumption of the lungs of the fetal lamb by multiplying the pulmonary blood flow by the arteriovenous oxygen difference. This calculation revealed that the lungs accounted for 8 percent of the total oxygen consumed. Carlyle (5) obtained a similar figure by placing fetal lung in the Warburg apparatus; when he studied the tissues of the adult sheep in the same manner, however, he found that the lung utilized only 1 to 4 percent of the total oxygen consumption.

The present approach has several limitations. One is that the technique ignores the role of anaerobic metabolism, and, while the importance of this role has not been established, the possibility that it has significance exists. A second limitation may be present if Thebesian veins carry venous blood into the left atrium or ventricle. In this situation the oxygen which the myocardium has extracted from the blood will be included in the calculated oxygen consumption of the lungs. Whereas the Thebesian veins represent only a potential source of error (6), larger systemic-pulmonary channels, such as those known to connect the chest wall and lungs through pleural adhesions or those thought to join the portal and pulmonary vessels in Laennec's cirrhosis, could introduce an error of considerable magnitude. This error would, however, be associated with a discrepancy between the outputs of the right and left ventricles (3), and since in this series comparisons of these outputs revealed an insignificant difference, any error from this source was probably small.

A third difficulty may be introduced by the dye curve used to measure the output of the right ventricle. A pre-

vious study demonstrated that curves drawn simultaneously either from the pulmonary and brachial arteries or from the two brachial arteries gave outputs which showed a satisfactory average agreement, yet occasionally differed by more than 10 percent (3). A final deficiency is one which is encountered in any calculation based on the relation between the oxygen consumption measured at the mouth and the rate at which oxygen enters the pulmonary capillaries. Extraneous factors, such as changes in the mean volume of the lungs during the period of measurement, can artificially influence this relationship.

As previously mentioned, the method cannot be used to study patients free of severe infection because such patients do not show a systematic difference between the Fick and dye-dilution outputs. While this is probably attributable to the fact that the oxygen consumption of the normal lung lies within the errors of the methods, it may also be due to the circumstance that the dye and Fick measurements are customarily made in sequence, rather than simultaneously. In an attempt to minimize the effects of these factors, we are investigating the feasibility of measuring \dot{Q}_R by infusing into the right atrium a solution containing an inert gas dissolved in saline. The principle of the method may be demonstrated by writing an equation similar to Eq. 1 written for oxygen. Thus

$$\dot{Q}_R C_{\bar{V}_K} + \dot{Q}_B C_{B_K} - \dot{V}_{E_K} - \dot{V}_{T_{A_K}} - \dot{V}_{T_{C_K}} - (\dot{Q}_R + \dot{Q}_B) C_{A_K} = 0 \quad (4)$$

where \dot{V}_{E_K} = rate of elimination of the gas in the expired air, and the other symbols correspond to those defined for oxygen. Rearranging, we have

$$\dot{Q}_R (C_{\bar{V}_K} - C_{A_K}) - \dot{V}_{E_K} + [\dot{Q}_B (C_{B_K} - C_{A_K}) - \dot{V}_{T_{A_K}} - \dot{V}_{T_{C_K}}] = 0 \quad (5)$$

In the steady state, the tissues are saturated and, because the gas is inert, $\dot{V}_{T_{C_K}}$ and $\dot{V}_{T_{A_K}}$ are zero. Further, $C_{A_K} = C_{B_K}$ so that the term $\dot{Q}_B (C_{B_K} - C_{A_K})$ becomes zero also. Hence

$$\dot{Q}_R = \frac{\dot{V}_{E_K}}{C_{\bar{V}_K} - C_{A_K}} \quad (6)$$

and, substituting Eq. 6 in Eq. 3 gives

$$\dot{V}_{T_{O_2}} = \dot{V}_{O_2} - \dot{V}_{E_K} \left[\frac{C_{A_{O_2}} - C_{\bar{V}_{O_2}}}{C_{\bar{V}_K} - C_{A_K}} \right] \quad (7)$$

In a similar manner, one can show that the carbon dioxide ($\dot{V}_{T_{CO_2}}$) pro-

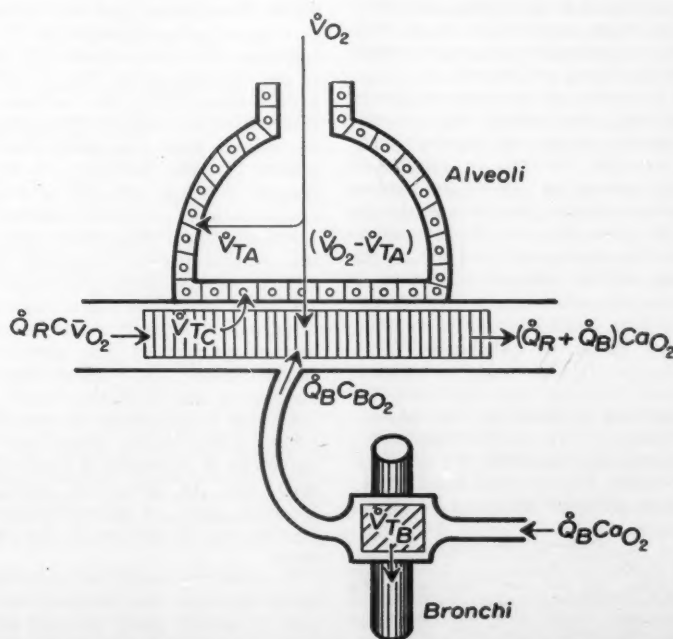


Fig. 1. Theoretical exchanges of oxygen within the lungs. For explanation of symbols, see text.

duced by the pulmonary tissues can be calculated from

$$\dot{V}_{\text{TCO}_2} = \dot{V}_{\text{CO}_2} - \dot{V}_{\text{EK}} \left[\frac{C_{\text{vCO}_2} - C_{\text{aCO}_2}}{C_{\text{vK}} - C_{\text{aK}}} \right] \quad (8)$$

where the symbols correspond to those defined for oxygen. And, finally, the respiratory quotient (R_T) of the tissues can be calculated by dividing Eq. 7 into Eq. 8.

$R_T =$

$$\frac{\dot{V}_{\text{CO}_2} (C_{\text{vK}} - C_{\text{aK}}) - \dot{V}_{\text{EK}} (C_{\text{vCO}_2} - C_{\text{aCO}_2})}{\dot{V}_{\text{O}_2} (C_{\text{vK}} - C_{\text{aK}}) - \dot{V}_{\text{EK}} (C_{\text{vO}_2} - C_{\text{aO}_2})}$$

In essence, this approach consists of simultaneously applying the Fick principle with two different gases. One of these, oxygen, is metabolized, while the other, an inert gas, is not.

The success of this approach hinges on the degree to which a steady-state can be approximated, particularly in regard to the equilibration of the gas with the tissues. If equilibrium cannot be achieved, \dot{Q}_R can still be estimated by substituting the rate of infusion for \dot{V}_{EK} in the last four equations, and by using the gas concentration in arterial blood as an estimate of that in the blood draining from the tissues into the right side of the heart. Results from this method with the inert gas Kr^{85} have been more reproducible than those obtained with dye. But whether the errors will be sufficiently minimized to assure the applicability of the technique to patients free of pulmonary infections is not yet known.

If the utility of the approach can be established, the method might provide information on several disputed points. For example, the role of metabolism in the genesis of pulmonary diseases might be studied, the effect of therapy on the metabolism of pulmonary lesions might be investigated, and the participation of the pulmonary tissues in diseases of metabolism, such as hyperthyroidism, might be explored (7).

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12 December 1960

Uptake of Tritium-Labeled Norepinephrine in Brain and Other Tissues of Cat in vitro

Abstract. Slices of cat cerebral cortex, heart, and spleen that have been incubated in media containing approximately 5 to 25 μg of *dl*-norepinephrine- 7H^3 per milliliter contain levels of isotopic amine greater than those in the medium. The effects of norepinephrine concentration, reserpine, and ouabain on the uptake suggest that the amine enters cells both by diffusion and by a concentrating mechanism that is saturated at low levels of norepinephrine. The drugs inhibit the latter.

Hughes and Brodie (1) have presented evidence that active transport of 5-hydroxytryptamine is an important factor in maintaining the high concentrations of this amine in blood platelets. The present studies were undertaken to determine whether a similar mechanism contributes to the relatively high levels of catecholamines maintained in parts of the brain and in sympathetically innervated organs (2).

Tissue slices were incubated in Krebs bicarbonate medium containing 5 μg of *dl*-norepinephrine- 7H^3 per milliliter. The concentration of isotope in cat cerebral cortex (Fig. 1) rose to several times that in the medium. Uptake curves for slices of hypothalamus, cerebellum, heart, and spleen were very similar to those in Fig. 1. Liver and muscle, however, did not accumulate concentrations of norepinephrine significantly greater than that in the medium. Approximately 75 percent of the radioactivity in cortex and heart after 1 hour of incubation was accounted for as unchanged norepinephrine by column chromatography of the contents of pooled slices (3). Chromatographic analysis of the incubation media indicated that 70 percent of the metabolites produced by cortical slices were 3,4-dihydroxy or 3-methoxy-4-hydroxymandelic acid. In the heart media the O-methyl ether of norepinephrine accounted for 60 percent of the metabolites.

In order to determine the effect of norepinephrine concentration on the rate of uptake, tissue levels of labeled norepinephrine were measured after 20 minutes of incubation, during which time the uptake is approximately linear.

The ratio of tissue concentration of isotope to concentration in the medium was maximal in cortex and heart at levels between 5 and 25 $\mu\text{g}/\text{ml}$. At higher levels the tissue concentration approached that of the medium. These data, which resemble those obtained with epinephrine (4), suggest that catecholamines, like 5-hydroxytryptamine in platelets (1), enter nervous tissue in two ways. At low levels of norepinephrine most of the inward flux would occur by a concentrating mechanism involving a carrier, presumably enzymatic. The data of Table 1 would be consistent with the saturation of such a carrier at norepinephrine levels of about 25 $\mu\text{g}/\text{ml}$ above which the rate of entry by this mechanism could not be further increased.

The second component of the inward flux would be a simple diffusion by which the internal concentration of the amine should gradually approach the external one. The rate of this process, however, should not be subject to an upper limit since diffusion rates vary linearly with concentration. Thus the limited quantity entering in a given time by the concentrating mechanism should become a negligible fraction of the much larger amounts forced through the diffusion barrier by very high external concentrations, and the ratios of Table 1 would be expected to approach unity.

Uptake of norepinephrine by the concentrating mechanism could represent either chemical binding to tissue components or active transport by an energy-requiring pump of low capacity. That it may be the latter is suggested by the marked inhibition of the inward flux by ouabain (Fig. 1), since cardiac

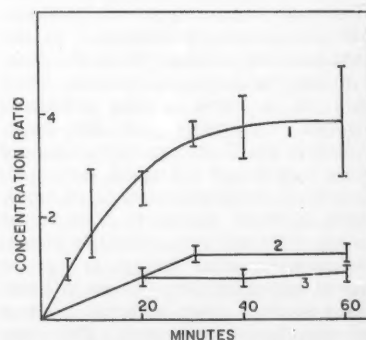


Fig. 1. Ratio of concentration of radioactivity in cat cerebral cortex slices to that in a Krebs bicarbonate medium containing 5 μg of *dl*-norepinephrine- 7H^3 per milliliter. Curve 1, control. Curve 2, 24 hours after reserpine (3 mg/kg) was injected intraperitoneally. Curve 3, slices from normal cats incubated in media containing 10^{-5}M ouabain. Vertical bars represent standard deviation of values obtained with tissues from eight cats.

Table 1. Ratio of concentration of radioactivity in cat cerebral cortex to that in Krebs bicarbonate medium after incubation of slices for 20 minutes at 37°C with *dl*-norepinephrine-7H³.

Concentration ($\mu\text{g}/\text{ml}$)	Ratios in	
	Normal medium	10 ⁻⁶ M reserpine
1	0.63	0.58
5	2.28	1.43
25	1.85	1.35
100	1.63	1.50
200	1.17	0.98

glycosides are known to block the utilization of metabolic energy for the active transport of a number of substances (5). Reserpine is reported to block the active transport of 5-hydroxytryptamine in platelets (1). In cortex slices from reserpinized animals (Fig. 1), as well as in those exposed to reserpine *in vitro* (Table 1), the tissue concentration of norepinephrine after incubation was reduced. Reserpine apparently blocks the concentrating mechanism since at the higher concentrations of norepinephrine where inward flux is primarily by diffusion the effect of the drug was considerably lessened.

In the presence of the sulfhydryl inhibitors, iodoacetate (10^{-3} M), and *p*-chloromercuribenzoate (5×10^{-6} M), norepinephrine uptake by cortex slices was reduced to 78 and 50 percent of control values. Dinitrophenol (10^{-3} M) reduced uptake by 25 percent. Fluoride and azide were without effect. Slices warmed at 55°C for 10 minutes in isotonic saline were unable to concentrate isotopic norepinephrine when incubated under the usual conditions.

Although isotope was more concentrated in tissue than in the medium after incubation, the concentration ratios were much lower than would be expected if there were complete isotopic exchange between extracellular and endogenous norepinephrine. Complete exchange between the radioactive norepinephrine in 3 ml of a solution containing 5 $\mu\text{g}/\text{ml}$ and the endogenous norepinephrine in a 100-mg slice of cortex (approximately 0.04 μg) (2) should yield a ratio of isotope concentration in tissue to that in the medium of about 75. Since experimentally this ratio has never exceeded 5.8 after 1 hour of incubation, the isotopic norepinephrine must exchange slowly, if at all, with the amine in intracellular storage sites. In adrenal medulla (6), splenic nerve (7), and perhaps in nervous tissue generally (8) these storage sites appear to be cytoplasmic granules. Adrenal medulla was unusual in that slices of this tissue did not concentrate labeled norepinephrine to levels significantly greater than in the medium.

This result is in keeping with Hillarp's observation (9) that isotopic epinephrine did not exchange with the epinephrine in isolated adrenal medullary granules, but seems surprising in view of the reported accumulation of isotopic norepinephrine in the rat adrenal after intravenous injection of small amounts (10).

It is possible that the concentrating mechanism delivers norepinephrine to an intracellular pool distinct from the particulate sites where much of the amine appears to be stored. Recent results of Burn and Rand would be consistent with the existence of such a pool (11).

A number of drugs that sensitize adrenergic organs to administered catecholamines inhibit uptake (12), by the concentrating mechanism observed here. It is possible that the latter represents a means for terminating the biological effect of catecholamines.

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Vessels in Roots of *Marsilea*

Abstract. The occurrence of vessel members in the roots and the possible occurrence of sieve-tube members in the rhizome is reported for the first time in the heterosporous fern *Marsilea quadrifolia*. This discovery adds a new instance of parallel evolution of vessels in vascular plants.

Vessel members, although highly characteristic of the flowering plants, occur also in other widely divergent groups of vascular plants (1) including the Selaginellales (*Selaginella*), the Equisetales [*Equisetum* (2)], the

Genetales (*Gnetum*, *Welwitschia*, and *Ephedra*), and the Filicales [in which they have previously been reported only in *Pteridium* (3)]. It is my purpose herein to record for the first time their occurrence in the roots of the heterosporous fern, *Marsilea quadrifolia*. This discovery is of unusual interest as another example of parallel evolution in vascular tissue.

The vessel members of *Marsilea* have distinct end walls and are superposed in vertical columns (Fig. 1c). The end walls vary from steeply oblique with scalariform perforations through a series of intermediate forms (Fig. 1a and b) to transverse end walls with a simple perforation. Often a single vessel member will show both extremes—the steep scalariform perforated wall at one end, and the transverse simply perforated wall at the other. The individual vessel members average 3.6 mm in length and 27.4 μ in width. Reduced scalariform pitting occurs on the lateral walls.

A test was made to determine whether particles of India ink would pass through these cells (4). The ends of decapitated roots were immersed in ink, and it was found that the ink particles pass readily throughout their length. As these particles are too large to pass through pit membranes, it was concluded that the conducting cells must be true vessel members. It is significant that no ink particles were conducted into the rhizome where the conducting elements were found to be tracheids.

An examination of two other species of *Marsilea* (*M. drummondii* and *M. hirsuta*) revealed that they also possess vessels in their roots, but, as in *M. quadrifolia*, they lack vessels in the rhizome and petiole. Additional species of *Marsilea* are currently under investigation.

No vessels were observed in any of the organs of species in the two other genera of the Marsileaceae, *Regnellidium* and *Pilularia*. Likewise, none were found in species of *Salvinia* and *Azolla* of the other heterosporous fern family, Salvinaceae.

It is interesting that in the course of this survey, cells with the appearance of true sieve-tube members were observed in the phloem of *Marsilea*. These cells, which are very long, have sieve areas restricted to oblique end walls, and only irregularly scattered simple pits have been observed on the lateral walls. They form continuous series of cells in the internodal regions of the rhizome. Peculiarly, the sieve-tube members are confined to the rhizome, which has only tracheids in the xylem. The roots, which have vessels in the xylem, have only typical sieve cells in the phloem. If these cells

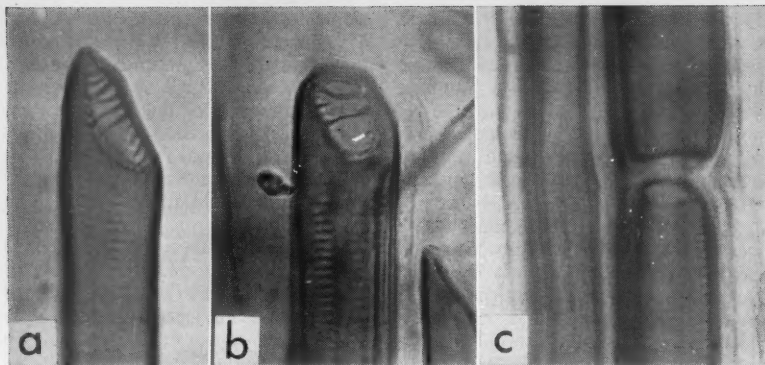


Fig. 1. Vessel members of *Marsilea quadrifolia*. Vessel members with scalariform-perforated end walls (a, b). The articulation of two vessel members with transverse, simple-perforated end walls (c).

are, indeed, sieve-tube members, their occurrence in *Marsilea* will be, as far as is known, unique within the Filicales and the only known occurrence outside of the angiosperms.

On the basis of frond form, *Marsilea* is generally regarded as the most primitive genus of the Marsileaceae. On the basis of sporangial type, however, *Marsilea* is evidently the most specialized (5). The evidence from the vascular tissue tends to support the latter.

The vessels of the bracken fern, *Pteridium*, are very different from those of *Marsilea*. They are located in the rhizome, petiole, and root and are not confined solely to the roots, as in *Marsilea*. Furthermore, the vessels of *Pteridium* possess members with only the scalariform type of perforation plate. Pits on the lateral walls are typically scalariform, whereas those of *Marsilea*, although scalariform, are relatively smaller and more widely spaced. In addition, vessel members in *Pteridium* are much shorter than those of *Marsilea*.

Both *Marsilea* and *Pteridium* are members of families considered to be taxonomically advanced. The heterosporous family Marsileaceae is generally considered more highly advanced than the Pteridaceae. The vessel members of *Marsilea*, on the basis of characters used to determine degree of specialization in angiosperms, are, with the exception of their length, more highly specialized than those in *Pteridium*.

The discovery of vessel members in *Marsilea* demonstrates once again the homoplastic development of these structures in taxonomically widely separated plants. In view of their occurrence in these distantly related genera, and the differences in morphology and location in the plant, it is probable that the vessels have originated independently at least twice in the ferns—in the terrestrial *Pteridium* and in the aquatic *Marsilea*. This parallels the situation

that seems to have occurred in the angiosperms (6).

Histological and developmental studies will supply detailed information concerning the nature and ontogeny of the vessel and supposed sieve-tube elements in *Marsilea*. A statistical study of the tracheary elements of the ferns in progress will provide a broader basis for a more critical interpretation of the significance of these cell types in the Filicineae (7).

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X-rays Affect the Incorporation of 5-Iododeoxyuridine into Deoxyribonucleic Acid

Abstract. When labeled with iodine-131, 5-iododeoxyuridine, an analogue of thymidine, is useful in estimating the effect of x-radiation on deoxyribonucleic acid metabolism. Although this compound is readily incorporated into deoxyribonucleic acid in the absence of ionizing radiation, we find that whole-body exposure to as little as 10 r will significantly inhibit its incorporation.

The debilitating effects of x-rays to higher animals are usually the delayed consequences of the inhibition of multiplication or death of cells in certain normally proliferative tissues. Tracer studies in turn suggest that the damage

to proliferating cells can be correlated with altered metabolism of their genetic material, deoxyribonucleic acid (DNA). Tritiated-thymidine, while an excellent measure of DNA metabolism (1), is difficult to assay because of the weak energy of tritium's β -radiation; whereas an iodinated analogue would permit easy assay of whole tissues or animals by the gamma rays of radioiodine. Therefore, the present technique was developed, utilizing the thymidine analogue, iododeoxyuridine (2), which can be incorporated in place of thymidine into DNA (3). For this purpose the iododeoxyuridine was prepared labeled with I^{131} by iodination of deoxyuridine as described by Prusoff (2) [but with the addition of radioactive iodine (I^{131}) to the reaction mixture] and purified by four recrystallizations from water.

Groups of Swiss albino mice, 6 to 10 weeks old, were exposed to 250 kv (peak) x-rays filtered through 0.5 mm. of copper and 1 mm. of aluminum. The rate of irradiation was 50 to 52 r/min, different doses being attained by varying the duration of exposure. At a variable time interval before the onset or after the cessation of irradiation, each mouse received a single intraperitoneal injection of 0.1 μ mole of the labeled compound having a specific activity of approximately 10 μ c/ μ mole; the controls were unirradiated litter mates, which had been similarly injected. All mice were given 0.1 percent NaI in their drinking water for at least 24 hours before injection with labeled iododeoxyuridine to prevent retention in the thyroid of radio-iodide, the major catabolic product.

The radioactivity of each mouse was counted periodically in a large well-type crystal scintillator. Figure 1 illustrates the average radioactivity retained (plotted logarithmically) by groups of three to five mice as a function of time after injection. In both irradiated and unirradiated animals the initial rapid disappearance of radioactivity was followed by a slow phase (from about the 10th to the 40th hour) in which the retained amount of activity remained essentially constant and can be attributed to label in metabolically stable DNA within new cells. The more rapid loss of radioactivity after 40 hours undoubtedly reflects the death of labeled cells. Chemical data in support of this interpretation are as follows.

At intervals, two or three mice from a group were killed, and their organs were either assayed for radioactivity directly or for activity insoluble in 10 percent trichloroacetic acid after homogenization, precipitation with this reagent, and washing until the supernatant contained less than 2 percent of the radioactivity of the precipitated

Table 1. Incorporation of I^{131} -iododeoxyuridine into DNA after irradiation. The figures represent percentages relative to incorporation into unirradiated controls at 20 hours after injection of the iododeoxyuridine (three to five mice per tabulated number).

Exposure (r)	Incorporation at intervals between x-radiation and injection (%)			
	2 hr	6 hr	24 hr	48 hr
10	110	68		
25	52	39		
52	37	29	102	
104	24	23	55	
208	20	23	43	
312	18		39	
416	12		26	
520	13		22	
624	12		20	62

tissue. This precipitate contains the DNA together with most of the tissue proteins. Analysis of various organs revealed that the amount of acid-insoluble radioactivity reached a maximum within an hour after injection of labeled iododeoxyuridine. The acid-soluble radioactivity after this period was primarily due to the presence of iodide, resulting from degradation of the labeled compound. By 20 hours, almost all the body radioactivity was insoluble in trichloroacetic acid. Of the radioactivity lost from the body, over 95 percent was excreted in the urine, largely as iodide.

The unirradiated animal, 21 hours after the injection of labeled iododeoxyuridine, retained an average of 8.3 percent of the injected dose. The retained activity was proportioned 41 percent to the gastrointestinal tract (none of this was in its contents), 21 percent to the skin (about half of this represented contaminating iodide), and 15 percent to the bones (including bone marrow). Only 2.7, 2.3, 1.7, and 1.1 percent were present in the skeletal muscles, liver, thymus, and spleen, respectively. While the rates at which radioactivity

disappeared from the various organs were quite different, the preponderance of radioactivity in the gut and the steepness of the decline from this compartment after 40 hours largely account for the shape of the curve for whole-body retention.

Since the extent of incorporation of labeled iododeoxyuridine in the intact mouse could not be determined until after the degradation products had been eliminated, the amount of radioactivity present at 20 hours was chosen as a measure of incorporation. Table 1 shows that the incorporation was a function of the irradiation dose and of the time between irradiation and injection. Maximum inhibition of iododeoxyuridine retention for any given x-ray dose occurred approximately 6 hours after irradiation and was already close to maximum 2 hours after irradiation. Recovery, in that iododeoxyuridine retention returned to normal, began within 24 hours after administration of 52 r, but was not yet complete even 48 hours after administration of 624 r.

The inhibition produced by the larger doses is even greater than the graph indicates, for an iodide retention curve would approximate that for labeled iododeoxyuridine after administration of 624 r, and in fact, over 80 percent of the radioactivity "incorporated" when the labeled compound was given 2 to 24 hours after 624 r of radiation was found in the skin, largely as iodide (4). The greatest inhibition of incorporation was suffered by the gastrointestinal tract, and the greatest recovery, 48 hours after irradiation with 624 r, also occurred in this organ, little or no incorporation then being observed in the spleen, lymph nodes, or thymus. These results parallel those recently reported by Nygaard and Potter (5) for the effect of x-rays on the incorporation of thymidine- $2-C^{14}$ into the DNA of rat intestine, thymus, and spleen.

Irradiation given 2 hours after the injection of I^{131} -iododeoxyuridine produced a small depression in the curve for retained radioactivity, and irradiation given 24 hours after injection produced barely detectable changes in the shape of the retention curve, indicating that early death of labeled cells can account for only a fraction of the inhibition observed. The maximum inhibition observed 6 hours postirradiation (Table 1) may result from inhibition of mitosis and the resultant depletion of the proliferating pool, since this interval is close to the generation time for the rapidly proliferating cells of the gut. However, inhibitions observed at earlier times (Fig. 1) obviously cannot be so explained and must therefore represent either a slowing of DNA synthesis within cells or a less efficient utilization of

label because of altered cell permeability or increased pool size of DNA precursors.

In any event, the sensitivity of iododeoxyuridine incorporation in mice to as little as 10 r of precedent x-radiation suggests the possibility of developing this technique as an index of radiation injury in man after either accidental or therapeutic exposure. Of course, the possible mutagenic effects of labeled iododeoxyuridine, either from the compound itself or from its radiation, must be considered in any such study (6).

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Fallout Radioactivity in Cattle and Its Effects

Abstract. The levels of strontium-90 and cesium-137 in cattle grazed on the Nevada Test Site and elsewhere in Nevada are similar to those in cattle from other parts of the country. Gastrointestinal absorption of the relatively large amounts of radioactive cerium-praseodymium, ruthenium-rhodium, and zirconium-niobium present in the rumina is very small. Zinc-65 made its first appearance in samples of muscle and liver in November 1958 and has persisted in later samplings. There has been no evidence of biological damage to date, either histologically or grossly.

In 1957, the U.S. Atomic Energy Commission authorized a project (1) to determine what effects, if any, the radioactivity produced in atomic bomb tests at the Nevada Test Site was having on cattle grazing in areas heavily contaminated by fallout as contrasted

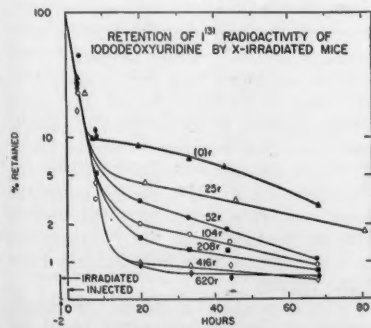


Fig. 1. Disappearance of total radioactivity in mice after injection of I^{131} iododeoxyuridine. Tracer was given 2 hours after x-radiation. "O" dose curve shows unirradiated controls. Three to five mice per point.

Table 1. Strontium-90 in grazing animals and in people.

No. of animals	Location *	Sample date	Sr ⁹⁰ /Ca (μμC/g)					Milk	Milk/bone	Ref.
			Rumen	Feces	Rib	Femur				
<i>Cattle</i>										
5	NTS	Fall 1957	436	602	13.9	15.6				
6	DV	Fall 1957	117	103	13.4	15.5				
4	NTS	Spring 1958		190	8.6	16.1				
3	DV	Spring 1958	56	62	17.6	15.5	3.1	0.19		
3	KC	Spring 1958	172	80	12.3	22.3	5.1	0.29		
4	NTS	Fall 1958	159	193	7.4	27.1				
4	DV	Fall 1958	57	55	9.6	14.3	1.8	0.15		
4	KC	Fall 1958	231	329	19.1	21.0	4.7	0.23		
<i>Sheep</i>										
	Br. Col., Can.	May 1956				32				(6)
	Chile	May 1956				7				(6)
	England	July 1957				200				(7)
<i>Caribou</i>										
	Alaska	May 1956			50-112					(6)
<i>Cattle</i>										
	Utah	Jan.-Apr. 1958					4.0			(3)
	Arizona	Jan.-Apr. 1958					1.0			(3)
	U.S. (av.)	1958					6.7-10			(4)
<i>Human beings (7-12 months)</i>										
	North America	1957-58				1.8				(8)

* NTS, Nevada Test Site; DV, Delamar Valley, Nev.; KC, Knoll Creek, Nev.

with cattle, at a distance, grazing on more normal pastures. Accordingly, 50 head of Hereford cattle, born and raised in the Delamar Valley just east-northeast of the Nevada Test Site, were purchased in November 1957; these animals were then grazed within the test site itself and comprised the maximum radiation exposure herd. A co-operative program was inaugurated with the University of Nevada to maintain two additional herds located at distances of 75 miles east (Delamar Valley, Caliente, Nevada) and 300 miles north (Knoll Creek, Contact, Nevada) of the test site. Twice yearly (May and November) five animals from

each herd were killed. Samples of bone, liver, muscle, thyroid, milk, rumen content, and feces were collected and radioassayed; a detailed autopsy was performed on each animal, and tissue sections were examined for histopathology (2). Film badges in small leather pouches on the neck chain of each animal were replaced bimonthly. Results of radioactivity analyses are summarized in Tables 1 and 2.

Considering the Sr⁹⁰ data first, it is clear that there are only small differences in the ratio of Sr⁹⁰/Ca among the three herds and between these cattle and grazing animals from other parts of the Northern Hemisphere. In fact, the

Nevada values are among the lower ones. The Southern Hemisphere value (Chile) is the lowest, which is consistent with world-wide fallout patterns. The values for human bone are less than those in any of the grazing animals, because of discrimination against strontium in moving up the food chain to man.

Milk samples also have Sr⁹⁰/Ca ratios close to the values for nearby Western states. The Nevada, Utah, and Arizona values are all similar and are less than the 1958 national average of 8.2 μC/g (4), which is what one would expect if most of the Sr⁹⁰ fallout comes from the stratospheric reservoir and is influenced on the local scale by rainfall patterns. The Sr⁹⁰/Ca ratio in milk is consistently lower than the ratio for bone in the Nevada cattle, the milk-to-bone ratio averaging about 0.2. Probably the milk-producing organs are better at rejecting Sr⁹⁰ than the bone; Comar (5) reports that in cows the ratio of Sr⁹⁰/Ca is 0.11 in milk and 0.18 in the skeleton.

The Sr⁹⁰/Ca ratio in the rumen and fecal samples, reflecting the Sr⁹⁰/Ca ratio in the feed shortly before slaughter, is higher than the bone values by something like an order of magnitude. In addition, these ratios are affected markedly by local fallout patterns and hence show larger fluctuations. Thus, the large Sr⁹⁰/Ca ratios in the 1957 samples is probably due to the Plumbob test series (spring and summer of 1957 at the Nevada Test Site); there was a reduction in the values in the spring of 1958 (a period of no testing).

The most striking feature of the results on γ-emitters is that the tissues contain so little radioactivity, in spite of the fact that the rumina contain relatively large amounts of the intermediate-lived fission products commonly found in dust and dirt. In Table 2, only Zr⁹⁵/Nb⁹⁵ values are listed; Ce¹⁴⁴/Pr¹⁴¹ values are similar, while Ru¹⁰⁶/Rh¹⁰⁶ are generally lower by a factor of 10. These are nonphysiological elements, and absorption through the gut wall is very small. Cesium-137, while certainly present, is swamped and not observed in the rumen contents, but is the main fission product in the samples of muscle and liver. It is significant that the Cs¹³⁷/K ratios are quite similar to those for commercial beef from widely separated locations. This means that the Cs¹³⁷ is coming mainly from the stratosphere, as was the case with Sr⁹⁰, and not from local fallout.

Fission product levels in the rumen contents and fecal samples from the Nevada Test Site herd showed a marked correlation with Nevada atomic bomb tests. The test series occurred during the spring and summer of 1957 (Plumbob) and in the fall of 1958

Table 2. Gamma-ray emitters in cattle. (N.D., not detected.)

Sample	Location *	Date	K ⁴⁰ (g K/kg)	Cs ¹³⁷ (μμC/g K)	Zn ⁶⁵ (μμC/kg)	Zr ⁹⁵ (μμC/kg)	Nb ⁹⁵ (μμC/kg)
Muscle	NTS	Dec. 1957	3.9	100	N.D.	N.D.	N.D.
	DV	Dec. 1957	3.8	93	N.D.	N.D.	N.D.
	Pooled	May 1958	3.9	120	N.D.	N.D.	N.D.
	Pooled	Nov. 1958	4.7	160	140	N.D.	N.D.
	Pooled	Nov. 1958	5.2	70	320	Trace	Trace
Bone	Pooled	Nov. 1958	Trace	Trace	Trace	N.D.	N.D.
Muscle (2-yr steer) (1-yr steer) (1-mo calf)	NTS	May 1959	2.8	122	107	N.D.	N.D.
	NTS	May 1959	3.0	76	77	N.D.	N.D.
	NTS	May 1959	4.5	112	153	N.D.	N.D.
Liver (2-yr steer) (1-yr steer) (1-mo calf)	NTS	May 1959	4.6	61	195	N.D.	N.D.
	NTS	May 1959	5.0	28	154	N.D.	N.D.
	NTS	May 1959	3.1	58	97	N.D.	N.D.
Hamburger	Local †	1959	2.3	87	30	N.D.	N.D.
Beef liver	Local †	1959	2.8	64	50	30	60
Rumen contents (av.)	NTS	Dec. 1957	N.D.	N.D.	N.D.	210,000	420,000
	DV	Dec. 1957	N.D.	N.D.	N.D.	35,000	70,000
	NTS	May 1958	N.D.	N.D.	N.D.	20,000	37,000
	DV	May 1958	N.D.	N.D.	N.D.	1,600	3,000
	KC	May 1958	N.D.	N.D.	N.D.	20,000	37,000
	NTS	Nov. 1958	N.D.	N.D.	N.D.	215,000	430,000
	DV	Nov. 1958	N.D.	N.D.	N.D.	58,000	116,000
	KC	Nov. 1958	N.D.	N.D.	N.D.	23,000	47,000

* NTS, Nevada Test Site; DV, Delamar Valley, Nev.; KC, Knoll Creek, Nev.

† Local purchase.

(Hardtack II), and the fission product levels in the Nevada Test Site herd were much higher in December 1957 and November 1958 than between tests (May 1958). The other two herds showed little change. This shows the effect of the relatively intense local fallout on the test site itself from smaller nuclear devices; this would be much more important for short-lived and intermediate-lived fission products than for the long-lived ones (such as Cs^{137} and Sr^{90} , the concentrations of which are not elevated in any of the three Nevada herds).

It is interesting that a new radioactivity, Zn^{65} , makes its first appearance in the November 1958 soft-tissue samples and remains present in the May 1959 samples. Zinc-65 is not a fission product, but is formed by neutron interaction on stable zinc. It has been detected in the general food supply (9), it is well absorbed from the gastrointestinal tract, and body retention is high (10). The amounts observed in the samples of liver and muscle were comparable to the Cs^{137} content.

External γ -ray dose and bone plutonium levels are trivial; the same was true of thyroid I^{131} levels with the exception of the Nevada Test Site herd soon after Hardtack II, when levels were of the order of the human maximum permissible level.

All reports from the Armed Forces Institute of Pathology indicate nothing significant from microscopic pathological examination. To date, no gross effects have been observed. The reproduction rate is normal, the animals are in a satisfactory state of nutrition, and there has been no increased incidence of any diseased condition.

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1. This work was performed under the auspices of the U.S. Atomic Energy Commission.
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18 August 1960

One-Trial Interhemispheric Transfer of a Learning Engram

Abstract. By using spreading depression to decorticate temporarily one hemisphere in rats, a learning trace was established in the opposite functional hemisphere. Spontaneous transfer of the engram from the trained hemisphere to the untrained hemisphere does not occur when both hemispheres are functional. If, however, the animal was allowed to make one reinforced response, complete transfer of the engram to the untrained hemisphere occurred.

We have been investigating (1) the use of spreading depression to decorticate temporarily one hemisphere and thereby to localize a conditioned performance to the other hemisphere as first described by Bures (2). This approach derives from the work of Sperry and his co-workers (3), who showed a similar localization of learning engrams in the split-brain preparation. In our technique, cups were implanted chronically around small holes drilled through the skull of male albino rats, one over each hemisphere. The dura was left intact. Plungers fitted into the cups prevented dehydration of the brain. A small pledget of cotton soaked with 25 percent potassium chloride was placed in the cup on one side to produce repetitive cycles of spreading depression restricted to that particular hemisphere. These spreading depressions inactivate the cortex for 3 to 4 hours (2).

The rats were given 1-hour daily sessions of operant training with one cortical hemisphere depressed. Under these conditions the functional cortex was exposed to bar-press conditioning under a continuous reinforcement schedule for food (4). In Fig. 1 the depressed cortical hemisphere is shown schematically, for each day, by cross-hatching.

On the first two days (Fig. 1), operant level scores were obtained, that is, measures of the animal's basal predisposition to respond without any training. On the 3rd and 4th days, the animal was reinforced for every response, and the increased rates indicate the animal had learned. The engram was

shown to have been established in the cortex that remained functional during training, when this trained cortex was depressed by spreading depression. This is shown in Fig. 1, for spreading depression was produced in the trained cortex on day 5, and the animal's response rate declined to a basal level. It should be noted that the responses on day 5 were not reinforced, and thus they were obtained under extinction conditions. On day 6 the trained cortex was again functional, spreading depression was initiated on the untrained side, and the return of a higher rate of responding coinciding with the functional return of the trained cortex indicates that the engram was not impaired by the presence of spreading depression on the previous day.

The procedure of trying the trained side and the untrained side under conditions of reinforcement and extinction was carried out on the same animal over a number of days (Fig. 1). On days 5 and 9 the amount of responding of the animal under extinction with the trained cortex depressed is shown. As has been noted, this performance does not differ from the operant level performance prior to conditioning. These extinction scores are in contrast with the score obtained on day 11, when the trained cortex was functional during extinction. The presence of an engram is shown in that hemisphere by the retention of learning in extinction.

This use of extinction tests as a retention measure of learning shows more rigorously the presence of a unilateral engram than does Bures's use of speed of learning scores, that is, the number of trials required to reach a criterion of conditioned performance. This operant technique is also flexible in terms

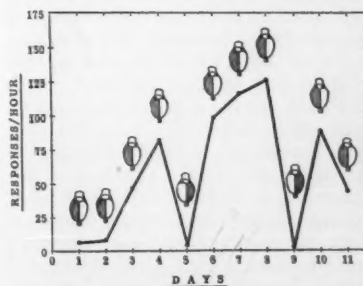


Fig. 1. Unilateral learning obtained by use of spreading depression as a technique of temporary decortication. The shading indicates the hemisphere depressed. The first two days give the operant level of responding before conditioning. Subsequent days show the increase in responding during training. On days 5, 9, and 11, responses are made during extinction. On days 5 and 9 the response level when the trained cortex is depressed is shown to be low as compared to day 11 when the trained cortex is functional.

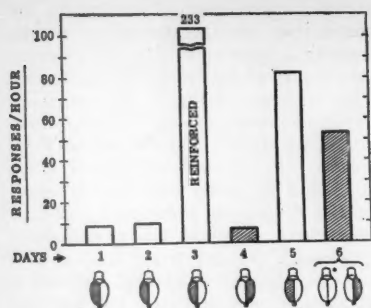


Fig. 2. Transfer of the learning engram to the untrained hemisphere. Days 1 and 2 give operant level, and day 3 shows the amount of responding made during training. The following days give the results of extinction tests. On day 4 the trained cortex is depressed, and day 5 shows the difference when the trained side is functional. On day 6 the animal was permitted to make one reinforced response with both hemispheres functional, and then 1 hour later the extinction test was given with the trained hemisphere depressed. The greater amount of responding indicates transfer has occurred after this single response.

of the kind of learning that can be established, and furthermore the presence or absence of a learning engram may be tested repeatedly over a number of days.

After recovering from spreading depression, the animal does not spontaneously transfer the engram to the other side, a point also noted by Bures. Our testing procedure extended over a week or two, and, despite this prolonged period, transfer still did not occur. If, however, an animal with a unilateral engram was allowed to make one response and receive one reinforcement while both cortical hemispheres were functional, transfer of the engram to the previously untrained side occurred.

An example of an animal demonstrating such one-trial transfer is shown in Fig. 2. On the first two days operant level performance was recorded with one hemisphere depressed. On the 3rd day the learning of a conditioned performance is demonstrated by the 233 reinforced responses made during 1 hour of conditioning. An extinction test was given on day 4 with the trained cortex depressed. The animal here performed at operant level indicating that no "learning" had occurred in the untrained side. On the 5th day the animal was tested in extinction with the trained cortex functional, and retention of training was shown by the animal's making 83 responses without reinforcement. This is well above operant level. The animal was permitted one reinforced response with both hemispheres functional on day 6. One hour later the animal was again tested, this

time with the trained cortex depressed. The extinction score of 56 responses indicates that transfer to the previously untrained side occurred and that one reinforcement was adequate to produce such transfer. The degree of success in training was tempered by the poor physical condition of the animals at the end of 2 weeks of continued elicitation of spreading depression, in view of which the positive evidence of one-trial transfer is additionally convincing. So far, 12 animals have shown unilateral learning, and an additional five have shown single-trial transfer.

These results are intriguing. The engram remains restricted to one hemisphere even though the neural connections for transfer are intact, and one single performance can result in transfer. It would seem that the animal does not transfer the engram without going through the actual behavior which is involved and that the "learning" of the engram by the untrained side takes place in an all-or-none fashion. This last point is of particular interest in connection with the work of Estes (5) whose recent psychological investigations led him, against his previous formulations, to think that learning is an all-or-none rather than an incremental process (6).

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Seasonal Evisceration in the Sea Cucumber, *Parastichopus californicus* (Stimpson)

Many species of sea cucumbers under rough handling will discard (eviscerate) their intestinal tracts and respiratory trees. For many years investigators at the Friday Harbor Laboratories of the University of Washington have noted occasional individuals of the large aspidochirote holothurian, *Parastichopus californicus* (Stimpson), which, when examined immediately after being dredged, lacked these organs. The gen-

Table 1. Presence or absence of intestine and respiratory trees in *Parastichopus californicus* collected at different seasons.

Date*	No. of animals	
	Complete viscera	Incomplete viscera†
2 Sept. 1959	12	0
28 Sept.	10	2
12 Oct.	8	4
26 Oct.	1	11
11 Nov.‡	0	25
10 Dec.‡	1	7
27 Dec.‡	1	0
22 Jan. 1960‡	17	0
3 and 5 Feb.	12	0
13 Feb.‡	5	0
4 March	12	0
18 March‡	23	0

* Also on 3 April, 30 April, 2 June, 4 July, and 3 August 1960, 12 specimens were collected, and all were found to have their viscera complete.
† Intestine and respiratory trees lacking or in early stages of regeneration. ‡ Groups of specimens dredged from deeper water.

eral assumption has been that these animals probably were stimulated to eviscerate by the mauling experienced in the dredge.

Some years ago in the late fall I collected a number of these animals from shallow water with a potato hook, brought them back to the laboratory in pails, and immediately opened them. The majority lacked the viscera mentioned above. The place of their collection was too shallow for dredging, and there was no reason to suspect that they had recently been handled by man, nor was there any evisceration after they were lifted from their habitat. Thus spontaneous evisceration, or at least evisceration in nature without stimulation caused by man's activities, was suspected.

In view of Bertolini's observations (1) on *Stichopus regalis* at Naples, which strongly suggests a seasonal evisceration in that species in late fall, the question arose as to whether or not *Parastichopus californicus* might not have a similar habit. Therefore, when an opportunity to spend another year at the Friday Harbor Laboratories (2) developed, plans were made for periodic collection of this animal from shallow water. As it appeared desirable to make all collections from the same locality, and because no readily accessible shallow-water area was found where the species occurred in very large numbers, each collection had to be limited in size.

Collections of 12 specimens each were made from a rowboat from low water to about 12 feet below that level with a long-handled potato hook. These animals were taken along the shore between the observation pier (48°32.7'N, 123°00.4'W) and a cove about ½-mile north (48°33.3'N, 123°00.3'W), known locally as Fern Cove. A summary of the findings is given in Table I.

Only one specimen eviscerated while being collected—the one noted as having viscera on 26 October 1959. Unfortunately, because of bad weather and unfavorable tidal conditions throughout the daylight hours, it was impossible to make the collections planned for near the beginnings of December and January. However, findings based on groups of specimens (indicated in Table 1 by ‡) dredged from deeper water within a few miles of this locality agree with what would have been expected. Thus it appears that *Parastichopus californicus* probably undergoes regular evisceration in the month of October and that within 1 to 3 months thereafter regeneration has proceeded sufficiently for the intestine to be functional as indicated by its being full of mud.

These findings are in close agreement with what Bertolini (1) found for *Stichopus regalis* and in contrast with Dawbin's (3) finding that in *S. mollis* evisceration appears to be a rare process. No experimental studies have been undertaken to determine rates or morphological details of regeneration, but the studies of Bertolini (4), Dawbin (5), Kille (6), and Mosher (7) suggest that such studies might yield interesting comparative data.

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30 December 1960

Radioactive Dating of Tertiary Plant-Bearing Deposits

Abstract. Four potassium-argon determinations from Tertiary rocks in the interior of British Columbia have yielded dates ranging from 45 to 49 million years. This suggests contemporaneity of three separate localities within the Middle Eocene epoch. Abundant plant micro- and macrofossils support this conclusion and indicate a flora quite different from floras of comparable age in western United States.

A more complete understanding of the Cenozoic history of the southern interior of British Columbia has long been hampered by the lack of a satisfactory local time scale, whereby isolated occurrences of Tertiary sediments

Table 1. A summary of localities, previous age determinations, source of samples, and potassium-argon (K-Ar) datings of Tertiary rocks from southern British Columbia. Constants: $\lambda_s = 0.589 \times 10^{-10}$ yr.; $\lambda_\beta = 4.76 \times 10^{-10}$ yr.; $K^{40}/K = 0.0118$ atomic percent.

Locality	Previous datings on fossil evidence	Source of biotite	K-Ar datings (10^6 yr)
Princeton (120½°W, 49½°N)	Late Eocene-Early Oligocene (5), Late Oligocene-Early Miocene (5), Oligocene or Miocene (5), Eocene (2, 5), Oligocene (5)	Volcanic ash	48
Tranquille (120½°W, 50¾°N)	Late Miocene (5), Miocene (5), Oligocene or Lower Miocene (5)	Diabase flow or sill	49
Savona Mountain (120¾°W, 50¾°N)	Datings same as for Tranquille	Trachyte flow	45
Rock Creek	Eocene (3), Upper Eocene-Oligocene (4)	Volcanic ash	49

and volcanics could be correlated with one another and with better-dated rocks of the western United States. Fossil plants, insects, fish, and mollusks have been collected at various localities, but they have provided no clear-cut evidence of age for any one series of rocks. The application of fossils to the dating of these rocks has been complicated by differences in latitude and environment from relatively well-dated collections to the south. Lithologic and stratigraphic correlations of volcanic rocks have led to confusion, and some successions originally correlated with Cenozoic strata have later been shown to be Cretaceous on paleontological evidence. Geomorphologic evidence of age is generally lacking and, even where present, has often been ignored or misinterpreted.

The development of the potassium-argon technique for dating has provided a new and useful tool for assisting in untangling the confused data and for the establishment of a stratigraphic column which is independent of the fossil record. Accordingly, we have embarked on a program for absolute dating through the collection of potassium-bearing rocks, with the ultimate objective of providing several well-dated horizons in the Tertiary sequence to which future paleobotanical, petrologic, tectonic, and geomorphologic evidence can be related.

To date, four age determinations from biotite-bearing rocks are considered most significant because of their intimate relationships to fossil-bearing strata (Table 1).

A potassium-argon date of 48 million years for the Princeton ash places it, according to recently proposed time scales (1), about the middle of the Eocene. This age accords well with that indicated by two sets of mammal teeth from a coal bed situated 100 feet above the ash bed. These teeth were identified by Russell and by Gazin (2) as remains of Middle Eocene trogonine tilodonts. This group of tilodonts is only known to range from uppermost Lower Eocene to upper Middle Eocene,

and the Princeton form is known only from Middle Eocene. The mutual agreement of isotope and fossil dates enhances the validity of both and clearly indicates that the age of at least this part of the Princeton succession is Middle Eocene.

In addition to providing an absolute datum from which to work, the present findings agree with the conclusions previously reached by one of us (G.E.R.) from a preliminary study of plant macro- and microfossils—namely, that the Princeton and Tranquille sediments contain synchronous floras. Similarly, evidence provided by an earlier report (3) on a florule near Rock Creek suggests that it also is synchronous with the Princeton and Tranquille floras.

The main difficulty in dating the floras from the Princeton, Tranquille, and other locales appears to result from the effects of quite different ecologic, physiographic, and latitudinal conditions from those which accompanied the development of well-dated Eocene floras in the southern and western United States. The Princeton and Tranquille sediments contain a preponderance of *Equisetum*, *Azolla*, *Metasequoia*, *Sequoia*, *Chamaecyparis*, *Pinus*, *Alnus*, *Corylus*, and *Juglans*, together with many other species of temperate association. This is in contrast to the generally subtropical to warm-temperate aspects of Eocene floras of the Gulf Coast and western United States. It seems apparent that there was a more dramatic change in the whole floral assemblage from southerly into more northerly latitudes during Middle Eocene times than has hitherto been suspected. This, in turn, would explain adequately the widely diversified datings which have been given by various paleontological investigators (3-5).

The Princeton and Tranquille floras appear to be most closely related to a florule reported from Republic, Washington, by Brown (6). This florule was considered to be older than the mid-Miocene Latah flora from Spokane; it was provisionally dated by Brown as early Miocene. Arnold (7), however,

refers to the Republic florule as Oligocene. The present evidence would suggest that the Republic florule is Eocene in age.

In terms of age, the Princeton and Tranquille floras are synchronous with that from the Green River formation of Wyoming and Colorado. However, there appears to be a fairly large discrepancy in the floral composition between the two. This is not surprising, inasmuch as there are some $4\frac{1}{2}^{\circ}$ of latitude between the two, together with unknown ecological and physiographical differences. The discrepancies in floras point out the continuing need for fundamental research on the extent of the effect which latitude, altitude, mountain barriers, climate, and other factors had on synchronous but geographically isolated floras of the Tertiary.

It is intended that the present program of potassium-argon dating should provide the basis for relating future paleontological and stratigraphical investigations. With several critical horizons now well established, it will be much easier to relegate more accurately many other sedimentary and volcanic series to the stratigraphic column. This, in turn, will greatly enhance our knowledge of the history of the Tertiary period in western North America (8).

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14 November 1960

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Effect of Electroconvulsive Shock on an Extinguished "Fear" Response

Abstract. To test Gellhorn's hypothesis that electroconvulsive shock reinstates extinguished responses, a conditioned "anxiety" response was established and then extinguished in rats. A series of treatments did not restore the extinguished "anxiety" response; in fact, control animals showed appreciable spontaneous recovery of the "anxiety" response while treated animals did not.

Studies reported by Gellhorn (1), and a later investigation by Hamilton and Patton (2), have shown that convulsions produced variously by Metrazol, insulin, or electroshock would reinstate previously inhibited (extinguished) conditioned responses. In these studies animals were trained to avoid shock by jumping from one compartment to another of a double grill box upon presentation of an auditory stimulus. The avoidance response, which was extinguished by means of a series of non-shock trials, reappeared after convulsive therapy.

Griffiths (3) later replicated this finding by using treadmill running to induce convulsive seizures. On the assumptions that the avoidance behavior in these studies was motivated by "fear" and that the effect of withholding the shock following acquisition was to extinguish a conditioned "fear" response, Griffiths inferred from his results that convulsions tend to reinstate the extinguished "fear."

The present study was intended as a test of this inference by a technique which was first described by Estes and Skinner (4). In this situation thirsty animals are trained to press a lever for a water reward; the fear response is then superimposed on the lever-pressing responding by pairing an auditory stimulus with a shock during the lever-pressing session. The "fear" response appears as a perturbation in the lever-pressing curve, accompanied by crouching, immobility, and usually defecation.

Twelve male albino rats, 60 days old at the start of the experiment, served as subjects. All animals were deprived of water for 48 hours. They were then placed in modified Skinner boxes in which they learned to press a lever, first for regular, and then for aperiodic, water reward. All sessions were of 8-hour duration and were run on alternate days. Animals received no water except that obtained in the experimental boxes.

The "fear" response or conditioned emotional response was superimposed on the lever-pressing habit as follows. While the animals were lever-pressing, a clicking stimulus was presented for

3 minutes and terminated contiguously with the delivery of a painful electric shock (1.5 ma) to the animals' feet. All animals received such conditioning trials every 20 minutes through the 8-hour session. Not all of these trials, however, were shock-reinforced during the 8-hour session. Only 50 percent of the conditioned stimuli were paired with the shock, in a mixed order.

The conditioned emotional or "fear" response, characterized by suppression of lever-pressing, piloerection, urination, and defecation was quantified in the following manner. A record was kept of the number of lever responses made by the animal in the 3-minute clicker period and the 3-minute period preceding the clicker. The magnitude of the "anxiety" response was measured in terms of a suppression ratio which was computed by dividing the number of responses made during the 3-minute clicker period by the number of responses made during the 3-minute period just preceding the clicker onset. Complete cessation of lever responding during the 3-minute clicker period yields a ratio of 0 and is taken to indicate a well-developed "fear" response. Unchanged output during the clicker yields a ratio of 1.00 and increased output a value greater than 1.00. Mean suppression ratio values were calculated for each 8-hour session for each animal. Animals received such conditioning trials for 23 successive days at which time all showed marked suppression of lever responding during the stimulus period.

The extinction procedure was the same as that during conditioning except that the shock was omitted. This procedure was maintained for seven successive days until the suppression ratio values for all animals approximated a value above .90.

Animals were then divided into experimental (six animals) and control (six animals) groups. The experimental animals were given 21 electroconvulsive shock treatments administered three per

Table 1. Suppression ratio values for the last conditioning session (I), the last extinction session (II), and the first trial of the recovery test after electroconvulsive shock (III).

Rat No.	I	II	III
<i>Treated group</i>			
AD 1	0.37	0.98	0.49
AD 5	.08	.84	1.00
AD 6	.16	.92	0.82
AD 10	.06	.91	.80
Mean	.17	.91	.78
<i>Control group</i>			
AD 4	0.15	0.72	0.06
AD 7	.37	.87	.00
AD 8	.12	.97	.00
AD 9	.06	.99	.02
AD 11	.05	.93	.04
Mean	.15	.90	.02

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day for 7 days; the control animals were left undisturbed in their home cages. All animals were given free access to food and water during the treatment period.

After treatment all animals (5) were deprived of water for 48 hours and then tested. The test procedure consisted of an 8-hour run with nonshock-reinforced presentations of the clicker every 20 minutes during the session.

As is shown in Table 1, all animals had low suppression ratio values on the last set of conditioning trials, indicating a high degree of acquisition of the "fear" response. On the last extinction session, suppression ratio values for all animals approached 1.00, indicating recovery of lever-pressing during presentations of the clicker stimulus. After the electroconvulsive shock period, however, clear differences are evident between the treated and the control animals on the first trial of the test session (6). Lever responding by all of the control animals was almost completely suppressed in the presence of the auditory stimulus, which was indicated by suppression ratio values ranging from .02 to .06. All treated animals, on the other hand, continued to press the lever during the stimulus presentation, as is reflected in the suppression ratio values which range from .49 to 1.00.

These results are in accord with previous findings (7, 8) which demonstrated that electroconvulsive shock would virtually eliminate a "fear" response of the type described in the present experiment. In fact, to the extent that the "fear" response is spontaneously recovered during the time interval of the treatment period (and the present findings indicate that this is considerable), this study is essentially similar to the studies of Brady *et al.* (7) which did not involve an extinction phase prior to administrations of electroconvulsive shock.

The present findings that electroconvulsive shock treatments do not reinstate extinguished "fear" responses appear to be in direct conflict with the findings of Gellhorn. This apparent conflict may result from the possibility that electroconvulsive shock treatments have at least two effects. One effect is to attenuate "emotional" responding. The second effect, suggested by observation of behavior following electroconvulsive shock, is to produce hyperirritability, which is manifested primarily in easily elicited and high-amplitude startle reactions. That this effect of electroconvulsive shock will facilitate avoidance responding of the kind studied by Gellhorn seems to be indicated by the results of a study by Gellhorn and Minatoya (9). These investigators reported: "A partial conditioning leading to an

average of only 20% positive responses in the control group causes 82% conditioned responses in the experimental group subjected to two hypoglycemics during the training period."

In the light of this evidence, and in view of the present findings, it would seem that convulsions do not reinstate extinguished responses in any general sense.

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30 December 1960

Possible Effect of Lethal Visible Light on Year-Class Fluctuations of Aquatic Animals

Abstract. Visible light killed the eggs and developing embryos of brook and rainbow trout. It is hypothesized that light could kill the eggs and embryos of all aquatic vertebrates and invertebrates. Adaptations minimize but do not completely block this lethal effect. Under some circumstances, visible light could cause heavy mortality in a new year-class of an aquatic animal.

Eggs of the brook trout, *Salvelinus fontinalis*, stripped from fish at the New York State hatchery at Cold Spring Harbor in November 1959 and retained in the hatchery troughs, suffered an unusually heavy initial mortality, estimated at over 90 percent, in contrast with a usual mortality for such an operation of about 10 percent. Experiments proved that the visible light from 40-watt cool-white fluorescent bulbs was responsible.

Similar results were reported by Handorf (1) with another species of salmonid, the rainbow trout, *Salmo irideus*. Handorf also found that the various components of white light showed a differential lethal effect on the fertilized eggs and embryos. The violet

and blue bands were highly lethal, while the green, yellow, and orange bands were progressively less lethal and of a much lower level of lethality. A greater resistance to the lethal effect of all bands of visible light was exhibited by the more intensely colored yellow eggs than by the paler eggs.

In nature, salmonid eggs are shielded from the light by the loose gravel of the stream bottom on which they are laid and with which they become covered during the spawning process. Also in nature, salmonid eggs are normally of a more pronounced yellow color than is usual with the eggs of hatchery fish. In the hatchery, it has been proved that direct sunlight kills salmon and trout eggs in a few minutes, while indirect daylight increases the mortality of eggs and embryos of the sockeye salmon (2). Although the lethal effect of direct sunlight might have been due to ultraviolet rays, the subdued indirect light entering a hatchery would be devoid of ultraviolet rays, and the increased mortality of the eggs and embryos must be attributed to natural visible light.

On the basis of these findings, it is hypothesized that visible light is potentially lethal to the fertilized egg and developing embryo of all fishes, other aquatic fishlike vertebrates, and aquatic invertebrates. However, through adaptive changes in the structure of the body and behavior of the adults and in the structure of the fertilized egg and embryo, the lethal effect of visible light has been minimized, at least under normal conditions. Obviously in ovoviviparous forms, the abdominal wall and the often heavily pigmented, coelomic lining shield the fertilized egg and embryo from the deleterious effects of light.

In oviparous forms, the spawning habits of the adults help to protect the eggs and embryos from the lethal effects of light. A large number of fishes and aquatic invertebrates spawn during 3 periods of the year when cloudy, windy, and rainy weather predominates. Such weather conditions, by increasing the turbulence and turbidity of the water, reduce the penetration of light. Also, most fishes and aquatic invertebrates spawn in the littoral and sublittoral zones. Here, submerged and floating algae in salt water, and vascular plants and algae in fresh water, together with suspended matter including phytoplankton, filter out the more lethal violet and blue components of light and permit the greatest penetration of the less lethal green light (3). In the shallower waters of the littoral zone and in some lakes and streams, plankton and organic stains color the water to such an extent that only orange or red light, of low lethality, penetrates.

In addition to this general adaptive

the last
infection
recov-
(III).

III

0.49
1.00
0.82
.80
.78

0.06
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.00
.02
.04
.02

spawning behavior to minimize exposure of the egg and embryo to deleterious light, more specific types of behavior have evolved in some forms for the same purpose. The covering of salmonid eggs with gravel from the stream bottom has already been described. Other fishes, with adhesive, demersal eggs, lay them under projecting stones or in crevices between them, on the stems and leaves of higher aquatic plants, or in clumps of algae. Some fishes build elaborate nests which cover the eggs and embryos. Still others lay their eggs in the empty shells of mollusks and remain coiled about them while they develop. Similar variations in spawning behavior occur in other aquatic animals besides the true fishes.

Aside from this adaptive spawning behavior, the eggs and embryos themselves have also become adapted to help withstand the injurious effect of visible light. Such adaptations would be the development of structures to disperse light or to prevent penetration of lethal rays. In the newly fertilized egg and in the early embryological stages, the small oil globules distributed throughout the yolk could help to disperse light. In later embryological stages the irregular surface of the embryo itself might contribute to this dispersion. The newly fertilized egg and the yolk and embryo of later stages are commonly tinged with yellow. This would act as a filter, permitting mostly the less lethal yellow light to penetrate. In the late stages of embryological development in fishes, large melanophores are common over such sensitive portions of the body as the brain, spinal cord, and abdominal cavity. Large xanthophores are frequently associated with these melanophores. Nicol (4) also reports that the chromatophores in decapod larvae and mysids are organized in definite neural and visceral groups.

If the hypothesis that visible light is potentially lethal to the fertilized egg and developing embryo of oviparous aquatic vertebrates and invertebrates is assumed to be correct, it can be concluded that all adaptations tend to minimize the lethal effect of the light, but do not give complete protection against it. The degree of mortality of the eggs and embryos caused by exposure to

deleterious visible light would vary with changes in the environment. Years in which the spawning season extended over a period with clear, sunny weather comparatively free of wind and rain might result in unusually clear water, greater penetration of lethal visible light, and poor survival of the progeny of many aquatic forms. Year-class fluctuations in aquatic organisms have been attributed to changes in a wide variety of biological and physicochemical conditions such as food, predation, disease, temperature, salinity, and currents. Yet frequently such fluctuations have shown either no relationship to or a poor correlation with these factors. It is suggested that in these instances visible light intensity might have been the unknown factor influencing year-class fluctuation.

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28 December 1960

Formation of Free Radicals in Tritiated H₂O and D₂O Ice

Abstract. By using tritium as an internal source of radiation, electron spin resonance spectra may be obtained for samples contained in glass without the usual disturbing effects due to irradiated glass. The production of OH and OD radicals in tritiated H₂O and D₂O ice may be readily demonstrated with this technique.

Most of the available data on the production of free radicals in H₂O and D₂O ice have been provided by electron spin resonance studies of samples irradiated by cobalt-60 γ -rays at liquid nitrogen temperature (1, 2).

By using tritium, the effects of much higher linear energy transfer may be investigated. Moreover, a given sample may be irradiated and its electron spin resonance spectrum may be examined,

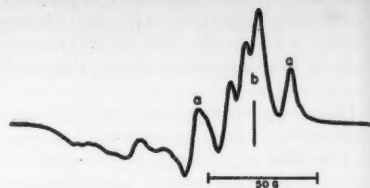


Fig. 1. OH doublet (a) and OD triplet (b) in electron spin resonance spectrum of tritiated H₂O and D₂O ice. The vertical line indicates the position of DPPH line. Field increases toward the right.

both in the same glass tube; thus one may obtain "pure" spectra of the materials under test without the usual disturbing effects due to irradiated glass.

An example of an electron spin resonance spectrum induced by T β -particles is shown in Fig. 1. The spectrum, representing the absorption derivative curve, has been recorded at liquid nitrogen temperature with an X-band Varian ESR spectrometer, model V4500, for a tritiated mixture of activity 1 c/ml, containing 80 percent H₂O and 20 percent D₂O.

The sample was kept over the period of about 2 weeks in liquid nitrogen, and the total dose of energy absorbed was 2.9×10^{20} ev/ml. Between the external peaks (Fig. 1, a) of the doublet, with separation approximately 40 gauss and g-value about 2.01, is situated a triplet (Fig. 1, b) with separation of 6 gauss.

By comparison with the data reported for cobalt-60 γ -rays (2), the doublet and triplet may be interpreted as due to OH and OD radicals, respectively (3, 4).

JERZY KROH

BASIL C. GREEN

JOHN W. T. SPINKS

Department of Chemistry, University of
Saskatchewan, Saskatoon, Canada

References and Notes

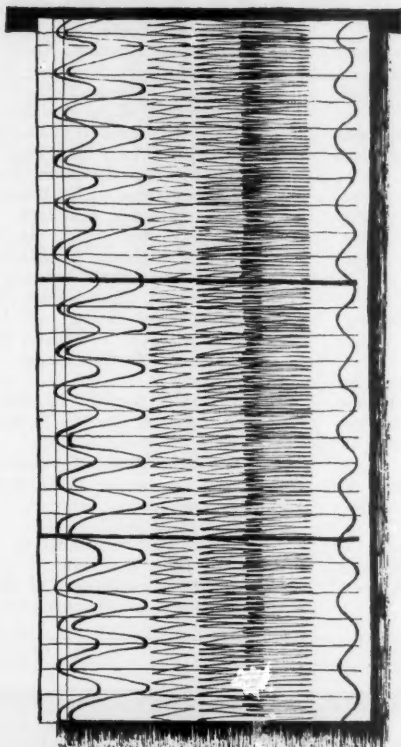
1. B. Smaller, M. S. Matheson, E. L. Yasaitis, *Phys. Rev.* 94, 202 (1954); S. M. Matheson and B. Smaller, *J. Chem. Phys.* 23, 521 (1955).
2. S. Siegel, L. H. Baum, S. Skolnik, J. M. Flournoy, *J. Chem. Phys.* 32, 1249 (1960).
3. A full description of these experiments and the production of H and D atoms in tritiated, acidified H₂O and D₂O is in preparation.
4. We are pleased to acknowledge financial assistance from the National Research Council of Canada.

2 December 1960

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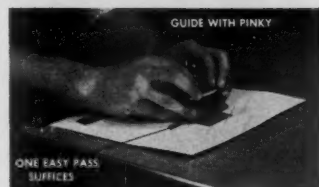
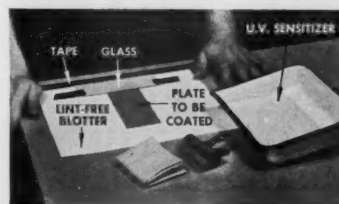
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Meetings

Forthcoming Events

April

27-5. American Psychiatric Assoc., annual, Philadelphia, Pa. (D. Blain, 1700 18 St., NW, Washington 6)

28-30. American Psychosomatic Soc., 18th annual, Atlantic City, N.J. (M. F. Reiser, 265 Nassau Road, Roosevelt, N.Y.)

30-4. Aero/Space Instrumentation Symp., 7th annual, Dallas, Tex. (W. J. Gabriel, Route 3, Box 36, Fort Worth, Tex.)

30-4. Electrochemical Soc., Indianapolis, Ind. (R. K. Shannon, 1860 Broadway, New York 23)

30-6. Conference on Internal Medicine, Nassau, Bahamas. (Bahamas Conferences, P.O. Box 1454, Nassau)

May

1-3. American Oil Chemists' Soc., St. Louis, Mo. (K. F. Mattil, Swift and Co., U.S. Yards, Chicago 9, Ill.)

2-3. American Pediatric Soc., Atlantic City, N.J. (C. M. Riley, Denver General Hospital, Denver 4, Colo.)

2-3. Association of American Physicians, Atlantic City, N.J. (P. B. Beeson, Yale Univ. School of Medicine, New Haven 11, Conn.)

2-5. Criticality Control in Chemical and Metallurgical Plant, intern. symp., OEEC, Karlsruhe, Germany. (European Nuclear Energy Agency, 38, Boulevard Suchet, Paris 16, France)

2-6. American Assoc. on Mental Deficiency, Cincinnati, Ohio. (N. A. Dayton, Mansfield Training School, Mansfield Depot, Conn.)

3-5. Nuclear Applications in Space Conf., Gatlinburg, Tenn. (J. J. Harford, American Rocket Soc., 500 Fifth Ave., New York, N.Y.)

3-6. American Goiter Assoc., Philadelphia, Pa. (J. C. McClintock, 702 Madison Ave., Albany 8, N.Y.)

3-6. Midwestern Psychological Assoc., Chicago, Ill. (I. E. Farber, Dept. of Psychology, State Univ. of Iowa, Iowa City)

3-7. Student American Medical Assoc., Chicago, Ill. (R. F. Staudacher, 430 N. Michigan Ave., Chicago 11)

4-5. Canadian Operational Research Soc., 3rd annual, Ottawa. (J. R. Walter, CORs, 800 Bay St., Toronto, Ont.)

4-5. Human Factors in Electronics, 2nd natl. symp., Arlington, Va. (H. P. Birmingham, Human Engineering Development Section, U.S. Naval Research Laboratory, Washington 25)

4-5. Society for Pediatric Research, Atlantic City, N.J. (C. D. West, Children's Hospital, Cincinnati 29, Ohio)

4-6. American Ethnological Soc., Columbus, Ohio. (Miss N. F. S. Woodbury, Arizona State Museum, Univ. of Arizona, Tucson)

4-6. American Philosophical Assoc., western division, St. Louis, Mo. (L. E. Hahn, Washington Univ., St. Louis 30, Mo.)

4-6. American Soc. of Human Genetics, Atlantic City, N.J. (W. J. Schull, 1133 E. Catherine St., Ann Arbor, Mich.)

4-6. New York State Psychological Assoc., annual, Rochester. (H. P. Iker, Strong Memorial Hospital, Room R-201, 260 Crittenden Blvd., Rochester 20)

4-6. Pediatric Surgery, symp., New York, N.Y. (Office of the Associate Dean, New York Univ. Post-Graduate Medical School, 550 First Ave., New York 16)

4-6. Society for American Archaeology, Columbus, Ohio. (J. B. Wheat, Univ. of Colorado Museum, Boulder)

4-7. Hypertension Symp. (by Hahnemann Medical College), Philadelphia, Pa. (Hahnemann Medical College and Hospital, 235 N. 15 St., Philadelphia 2)

5-6. Population Assoc. of America, New York, N.Y. (K. B. Mayer, Dept. of Sociology and Anthropology, Brown Univ., Providence 12, R.I.)

5-7. American Soc. of Internal Medicine, Miami Beach, Fla. (G. T. Bates, 350 Post St., San Francisco 8, Calif.)

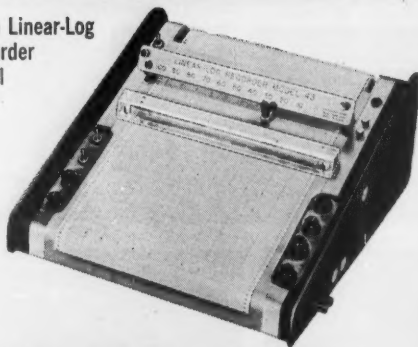
5-7. Wisconsin Acad. of Sciences, Arts, and Letters, 91st annual, Waukesha. (T. J. McLaughlin, Secretary, 2865 N. Prospect Ave., Milwaukee, Wis.)

5-8. American Psychoanalytic Assoc., Chicago, Ill. (Mrs. H. Fischer, 1 E. 57 St., New York 22)

6-7. Academy of Psychoanalysis, an-

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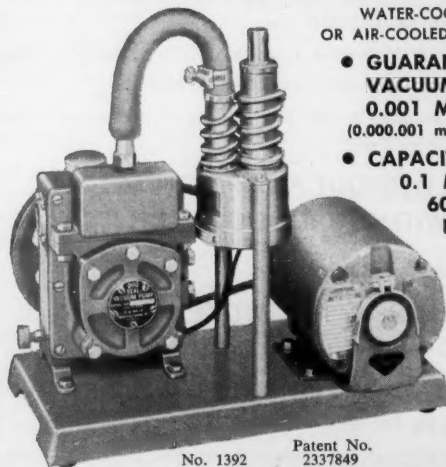
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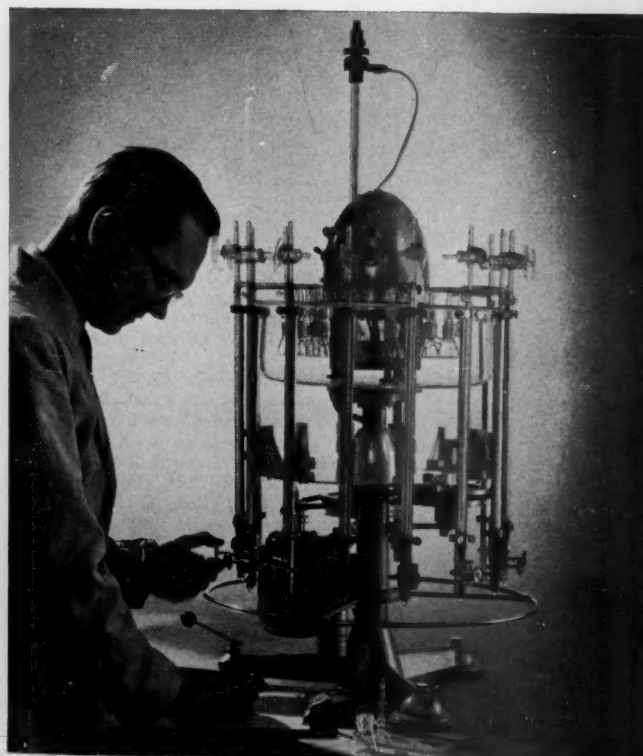
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6-9. Circuit Theory, 5th midwestern symp., Urbana, Ill. (M. E. Van Valkenburg, Dept. of Electrical Engineering, Univ. of Illinois, Urbana)

7-10. American Inst. of Chemical Engineers, Cleveland, Ohio. (J. F. Van Antwerpen, ALChE, 25 W. 45 St., New York 36)

7-11. Institute of Food Technologists, New York, N.Y. (C. S. Lawrence, 176 W. Adams St., Chicago 3, Ill.)

7-12. Medical Library Assoc., Inc., Seattle, Wash. (Miss R. J. Mann, Mayo Clinic Library, Rochester, Minn.)

7-12. Society of American Bacteriologists, 62nd annual, Kansas City, Mo.

(E. M. Foster, 311 Bacteriology, Univ. of Wisconsin, Madison 6)

7-12. Society of Motion Picture and Television Engineers, Toronto, Canada. (SMPTE, 55 W. 42 St., New York 36)

8-9. Titrimetric Methods of Analysis, symp., Cornwall, Ontario, Canada. (J. R. McCallum, Courtaulds (Canada) Ltd., Cornwall)

8-10. Aerospace Electronics Conf., 13th annual natl., Dayton, Ohio. (R. G. Stimmel, Institute of Radio Engineers, 1 E. 79 St., New York 21)

8-10. Instrument Soc. of America, Power Instrumentation Symp., 4th natl., Chicago, Ill. (H. A. Van Wassen, Duquesne Light Co., Pittsburgh 19, Pa.)

8-10. Mathematical Theories of Bio-

logical Phenomena, symp., New York, N.Y. (N. Rashevsky, Committee on Mathematical Biology, 5741 Drexel Ave., Chicago 37, Ill.)

8-12. American College of Physicians, 42nd annual, Miami Beach, Fla. (ACP, 4200 Pine St., Philadelphia 4, Pa.)

8-12. American Psychiatric Assoc., 117th annual, Chicago, Ill. (C. H. H. Branch, 156 Westminster Ave., Salt Lake City, Utah)

9-11. Western Joint Computer Conf., Los Angeles, Calif. (W. F. Bauer, 8433 Fallbrook Ave., Canoga Park, Calif.)

10-12. Production Engineering Conf., Toronto, Canada. (R. B. Larson, 5701 Carnegie Ave., Cleveland 3, Ohio)

10-13. National Science Fair—International, 12th, Kansas City, Mo. (Science Service, 1719 N Street, NW, Washington 6, D.C.)

11-13. Acoustical Soc. of America, Philadelphia, Pa. (W. Waterfall, 335 E. 45 St., New York 17)

11-13. American Inst. of Industrial Engineers, annual, Detroit, Mich. (W. J. Jaffe, Newark College of Engineering, 367 High St., Newark 2, N.J.)

11-13. American Radium Soc., Colorado Springs, Colo. (C. G. Stetson, 350 Engle St., Englewood, N.J.)

15-16. Co-ordination Compounds, symp., Hamilton, Ontario, Canada. (R. J. Gillespie, McMaster Univ., Hamilton)

15-17. Institute of Radio Engineers, natl. symp., Washington, D.C. (G. Shapiro, National Bureau of Standards, Washington 25)

15-17. Radiation Research Soc., annual, Washington, D.C. (E. L. Powers, Div. of Biological and Medical Research, Argonne National Laboratory, Argonne, Ill.)

15-18. Society of Aeronautical Weight Engineers, Akron, Ohio. (D. B. Block, 4004 Oxford Ave., NW, Massillon, Ohio)

15-18. Spectroscopy, 12th annual symp., Chicago, Ill. (W. Ashby, Continental Can Co., Inc., 7622 S. Racine Ave., Chicago 20, Ill.)

15-20. Conference on Nuclear Electronics, Belgrade, Yugoslavia. (J. Burl, International Atomic Energy Agency, United Nations, New York, N.Y.)

16-18. Western Conf. on Anesthesiology, biennial, Portland, Ore. (J. O. Brantford, 2307 NW Overton St., Portland 9, Ore.)

17-20. American College of Cardiology, New York, N.Y. (P. Reichert, 350 Fifth Ave., Empire State Bldg., New York 1)

18-20. Host Tumor Interactions, intern. symp., Detroit, Mich. (M. J. Brennan, Oncology Div., Henry Ford Hospital, Detroit 2)

22-24. American Thoracic Soc., Cincinnati, Ohio. (F. W. Webster, 1790 Broadway, New York 19)

22-24. Global Communications, 5th natl. symp., Chicago, Ill. (R. D. Slayton, 5555 Touhy Ave., Skokie, Ill.)

22-24. Telemetering Conf., natl., Chicago, Ill. (J. Becker, AC Spark Plug Division, General Motors Corp., Milwaukee 1, Wis.)

22-25. American Urological Assoc., Los Angeles, Calif. (W. P. Didusch, 1120 N. Charles St., Baltimore 1, Md.)

(See issue of 17 March for comprehensive list)

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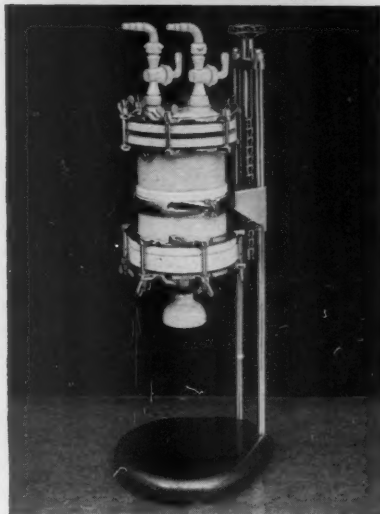
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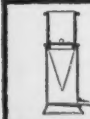
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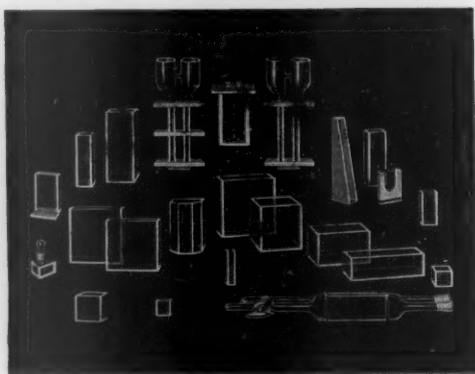
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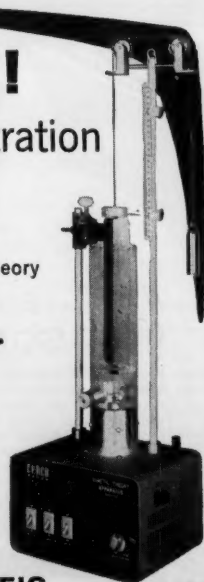
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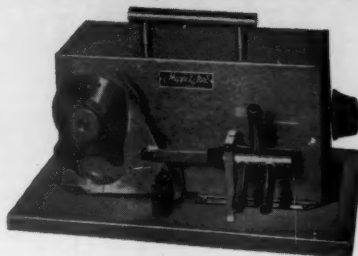
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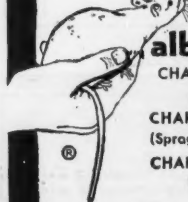
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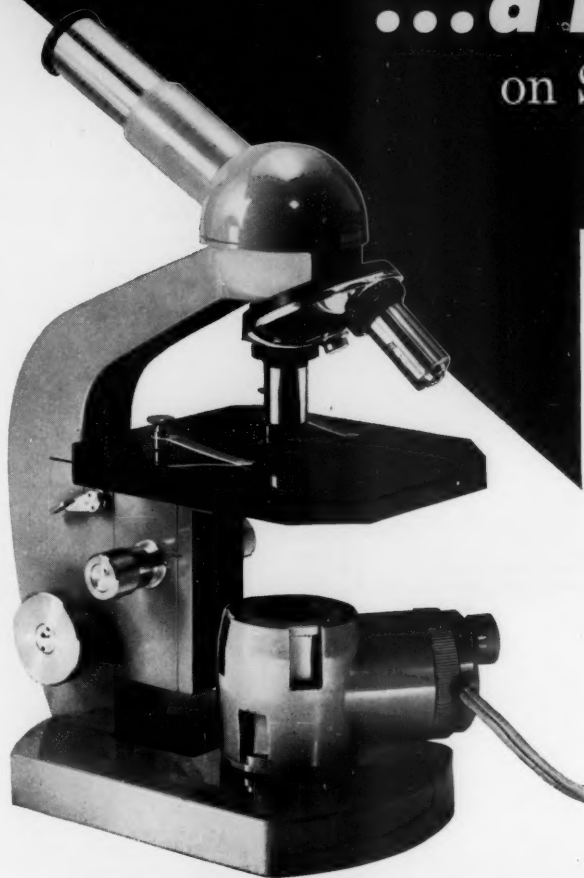
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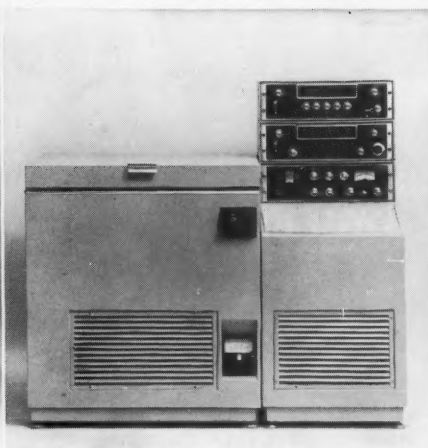
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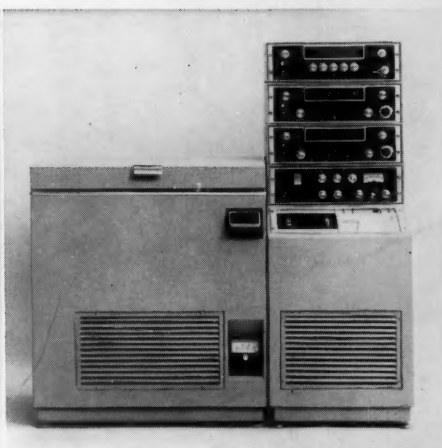
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